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Adams

STIC-ILL

Fr m: Wessendorf, Theresa
Sent: Monday, June 25, 2001 2:52 PM
To: STIC-ILL
Subject: 09/408,578

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Vaccine (1997), 15(14), 1551-1557.
Txs.
T. Wessendorf
Art Unit 1627
Mailrm. 3B01
308-3967

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Search Results -

Terms	Documents
l3 and (muliple adj3 antigen)	0

Database:
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- US Pre-Grant Publication Full-Text Database
- JPO Abstracts Database
- EPO Abstracts Database
- Derwent World Patents Index
- IBM Technical Disclosure Bulletins

Refine Search: `l3 and (muliple adj3 antigen)` Clear

Search History

Today's Date: 6/25/2001

DB Name	Query	Hit Count	Set Name
USPT	l3 and (muliple adj3 antigen)	0	L12
USPT	l3 and (muliple adj3 antigen adj3 system)	0	L11
USPT	l3 and (ligand adj3 presentation adj3 assembly)	0	L10
USPT	l1 and (ligand adj3 presentation adj3 assembly)	0	L9
USPT	l1 and (multiple adj3 antigen)	22	L8
TDBD	borrelia adj5 burgdorferi	0	L7
PGPB	borrelia adj5 burgdorferi	0	L6
EPAB	borrelia adj5 burgdorferi	70	L5
JPAB	borrelia adj5 burgdorferi	5	L4
DWPI	borrelia adj5 burgdorferi	119	L3
DWPI	l1	0	L2
USPT	borrelia adj5 burgdorferi	292	L1

STIC-Biotech/ChemLib

From: Wessendorf, Theresa
Sent: Monday, June 25, 2001 3:31 PM
To: STIC-Biotech/ChemLib
Subject: 09/408,578

Please search for Seq. ID. 1 with the terms multiple antigen or peptide system or ligand presenting assembly. Also, inventors' search.

Thank you
T. Wessendorf
Art Unit 1627
Mailrm. 3B01
308-3967

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FILE LAST UPDATED: 25 Jun 2001  (20010625/ED)

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=> d stat que l3
L1            83 SEA FILE=REGISTRY ABB=ON  PLU=ON  PVVAESPKKP/SQSP
L2            24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1
L3             2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2 AND (MULTIPLE(W)ANTIGEN OR
                 PEPTIDE(W)SYSTEM OR LIGAND)


=> d ibib abs hitrn l3 1-2

L3   ANSWER 1 OF 2  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2000:569091  HCAPLUS
DOCUMENT NUMBER:          133:265384
TITLE:                    Ligand-presenting assembly: a method for C-
                          and N-terminal antigen presentation
AUTHOR(S):                Holm, A.; Jorgensen, R. M.; Ostergaard, S.; Theisen,
                          M.
CORPORATE SOURCE:         Research Center for Medical Biotechnology, Chemistry
                          Department, The Royal Veterinary and Agricultural
                          University, Copenhagen, DK-1871, Den.
SOURCE:                   J. Pept. Res. (2000), 56(2), 105-113
                          CODEN: JPERFA; ISSN: 1397-002X
PUBLISHER:                Munksgaard International Publishers Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Achiral dicarboxylic acids were coupled with 2 equiv. of the free
     .alpha.-amino groups of two fully side-chain protected peptide chains
     while these were still attached to a synthesis resin.  Cleavage from the
     resin with simultaneous side-chain deprotection afforded two assembled
     peptide chains with free C-terminals.  Suitable functionalization of the
     achiral dicarboxylic acid alternatively permitted continued peptide
     synthesis in a C to N orientation leading to a final peptide assembly
```

which, after cleavage from the resin, may have multiple N to C and C to N presentation of one or more epitopes.

IT **262859-56-3P**
RL: ARG (Analytical reagent use); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(prepn. and application in ELISA)

IT **263013-02-1P**
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and immunogenicity of)

IT **262859-57-4P 262859-58-5P 262859-59-6P**
263013-01-0P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

REFERENCE COUNT: 16
REFERENCE(S): (1) Aletras, A; J Peptide Protein Res 1995, V45, P488 HCAPLUS
(2) Bhatnagar, P; J Med Chem 1996, V39, P3814 HCAPLUS
(3) Brandt, L; J Immunol 1996, V157, P3527 HCAPLUS
(5) Keah, H; J Peptide Res 1998, V51, P2 HCAPLUS
(6) Kim, H; J Med Chem 1994, V37, P3373 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:227676 HCAPLUS
DOCUMENT NUMBER: 132:250004
TITLE: **Ligand** presenting assembly (LPA), method of preparation and uses thereof
INVENTOR(S): Holm, Arne; Jorgensen, Rikke Malene; Ostergaard, Soren; Theisen, Michael
PATENT ASSIGNEE(S): Statens Serum Institut, Den.
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018791	A1	20000406	WO 1999-DK510	19990929
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9960783	A1	20000417	AU 1999-60783	19990929

PRIORITY APPLN. INFO.: DK 1998-1233 A 19980929
WO 1999-DK510 W 19990929
OTHER SOURCE(S): MARPAT 132:250004

AB The present invention relates to a method for prepg. a **Ligand** Presenting Assembly (LPA), an LPA, an immunol. compn. and a vaccine. The N-terminal of LPA is coupled to an achiral di, tri, or tetra-carboxylic acid so as to provide a construct having a ring structure. The invention further relates to a method for generating antibodies, a kit for use in diagnosis and use of an LPA for prepg. a pharmaceutical compn.

IT **262859-56-3P**, LPA-I **262859-57-4P**, LPA-II

262859-58-5P, LPA-III **262859-59-6P**, LPA-IV
263013-01-0P 263013-02-1P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**ligand** presenting assembly comprising achiral carboxylic acid-modified antigen as vaccine for diagnosis of infections)
IT **199437-17-7**, Pvvaespkkp peptide+
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**ligand** presenting assembly comprising achiral carboxylic acid-modified antigen as vaccine for diagnosis of infections)
REFERENCE COUNT: 7
REFERENCE(S):
(1) Anthony, G; WO 9402506 A 1994 HCAPLUS
(2) Golding Louise; WO 9832469 A 1998 HCAPLUS
(3) Harboe, M; INFECTION AND IMMUNITY 1998, V66(2), P717 HCAPLUS
(4) Peluso, S; TETRAHEDRON 1997, V53(21), P7231 HCAPLUS
(5) Statens Seruminstitut; WO 9742221 A 1997 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> d stat que l4
L1          83 SEA FILE=REGISTRY ABB=ON  PLU=ON  PVVAESPKKP/SQSP
L2          24 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L1
L3           2 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L2 AND (MULTIPLE(W)ANTIGEN OR
               PEPTIDE(W)SYSTEM OR LIGAND)
L4          12 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L1 AND (ANTIGEN? OR ASSEMBL?
               OR LPA?)) NOT L3


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=> d ibib abs hitrn l4 1-12

L4   ANSWER 1 OF 12  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:        2001:190694  HCAPLUS
DOCUMENT NUMBER:         134:339287
TITLE:                   Selection of continuous epitope sequences and their
                         incorporation into poly(ethylene glycol)-peptide
                         conjugates for use in serodiagnostic immunoassays:
                         application to Lyme disease
AUTHOR(S):               Qiu, Bo; Brunner, Michael; Zhang, Guobao; Sigal,
                         Leonard; Stein, Stanley
CORPORATE SOURCE:        Center for Advanced Biotechnology and Medicine,
                         Piscataway, NJ, 08854, USA
SOURCE:                  Biopolymers (2001), 55(4), 319-333
                         CODEN: BIPMAA; ISSN: 0006-3525
PUBLISHER:               John Wiley & Sons, Inc.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Continuous epitope sequences were selected from immunogenic Bb proteins by
     epitope mapping.  The identified epitope sequences were synthesized by
     solid phase peptide synthesis and purified by high performance liq.
     chromatog.  Each epitope was conjugated individually to a multifunctional
     poly(ethylene glycol) (PEG) carrier.  The result PEG-peptide conjugates
     were used as antigens in ELISA for diagnosis of Lyme disease.
     The results showed that the defined epitope peptides were Lyme disease
     specific and could be used in a format of PEG-peptide conjugate as the
     antigen to achieve improved sensitivity and specificity.
IT   338741-11-0D, polyethylene glycol conjugates
```

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (polyethylene glycol-peptide conjugates for use in serodiagnostic immunoassay of Lyme disease)

REFERENCE COUNT: 26

REFERENCE(S):
(3) Cartwright, G; J Immunol Methods 1995, V179, P31 HCAPLUS
(5) Fikrig, E; Proc Natl Acad Sci USA 1993, V90, P183 HCAPLUS
(6) Geysen, H; Proc Natl Acad Sci USA 1984, V81, P3998 HCAPLUS
(8) Kaiser, E; Anal Biochem 1970, V34, P595 HCAPLUS
(9) Mathiesen, M; Infect Immun 1998, V66(9), P4073 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:98788 HCAPLUS

DOCUMENT NUMBER: 132:150602

TITLE: Uses of borreliacidal epitopes of Borrelia burgdorferi outer surface protein C (OspC) in vaccines

INVENTOR(S): Callister, Steven N.; Lovrich, Steven D.; Schell, Ronald F.; Jobe, Dean A.

PATENT ASSIGNEE(S): Gundersen Lutheran Medical Foundation, Inc., USA

SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000006745	A1	20000210	WO 1999-US17270	19990730
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9953282	A1	20000221	AU 1999-53282	19990730
US 6210676	B1	20010403	US 1999-364083	19990730
EP 1100922	A1	20010523	EP 1999-938897	19990730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001000412	A	20010329	NO 2001-412	20010124

PRIORITY APPLN. INFO.: US 1998-94955 P 19980731
WO 1999-US17270 W 19990730

AB An epitope of the outer membrane protein C (OspC) of Borrelia burgdorferi is described for the prevention, treatment and early diagnosis of Lyme disease in humans and other animals. This invention also relates to a screening method detecting anti-Osp borreliacidal antibody activity, and antibodies reacting with a protein fragment encoded by a DraI-SmaI DNA fragment of the OspC gene. The OspC gene was cloned and deletion anal. was used to identify the region of the gene encoding a borreliacidal epitope. Borreliacidal antibodies to OspC were found in the serum of early Lyme disease patients and absorption of the serum with the OspC epitope lowered the borreliacidal activity 32-512-fold.

IT **257260-46-1**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological

study); PROC (Process); USES (Uses)
(amino acid sequence; uses of borreliacidal epitopes of Borrelia burgdorferi outer surface protein C (OspC) in vaccines)

IT **257289-49-9**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(epitope of OspC gene product of Borrelia; uses of borreliacidal epitopes of Borrelia burgdorferi outer surface protein C (OspC) in vaccines)

REFERENCE COUNT: 2
REFERENCE(S): (1) Immuno Ag; WO 9425596 A 1994 HCAPLUS
(2) Statens Seruminstitut; WO 9742221 A 1997 HCAPLUS

L4 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:809492 HCAPLUS
DOCUMENT NUMBER: 132:148850
TITLE: Genetic analysis of Borrelia garinii OspA serotype 4 strains associated with neuroborreliosis: evidence for extensive genetic homogeneity
AUTHOR(S): Marconi, R. T.; Hohenberger, S.; Jauris-Heipke, S.; Schulte-Spechtel, U.; LaVoie, C. P.; Rossler, D.; Wilske, B.
CORPORATE SOURCE: Medical College of Virginia at Virginia, Commonwealth University, Richmond, VA, 23298-0678, USA
SOURCE: J. Clin. Microbiol. (1999), 37(12), 3965-3970
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Infection with Borrelia garinii outer surface protein (Osp) A serotype 4 strains has been correlated with the development of neuroborreliosis in Lyme borreliosis patients in Europe. OspA serotype 4 isolates have been recovered primarily from human cerebrospinal fluid, suggesting a tropism for this environment. Previous studies with monoclonal antibodies directed against OspA and OspC demonstrated that OspA serotype 4 strains are **antigenically** closely related. In view of the pronounced **antigenic** and genetic variability that has been noted in the Osps of other Borrelia isolates, we sought to det. if OspA serotype 4 strains represent a recently emerged clonal lineage of B. garinii. Toward this goal, a representative group of OspA serotype 4 strains was analyzed for traits that typically exhibit hypervariability among isolates that cause Lyme borreliosis. The following criteria were assessed: (1) ospC sequences, (2) plasmid compn., (3) genomic restriction fragment length polymorphism (RFLP) patterns, and (4) the RFLP patterns of the upstream homol. box (UHB) element which flanks members of the UHB gene family at their 5' end. Collectively, these analyses demonstrate genetic homogeneity, suggesting that OspA serotype 4 strains are a recently emerged clonal lineage with an apparent tropism for the central nervous system.

IT **169539-68-8**, Protein (Borrelia garinii strain PTrob gene ospC outer surface)
RL: PRP (Properties)
(amino acid sequence; genetic anal. of Borrelia garinii OspA serotype 4 strains assocd. with neuroborreliosis: evidence for extensive genetic homogeneity)

REFERENCE COUNT: 63
REFERENCE(S): (2) Baranton, G; Int J Syst Bacteriol 1992, V42, P378 HCAPLUS
(4) Barbour, A; J Bacteriol 1996, V178, P6635 HCAPLUS
(5) Barbour, A; J Clin Microbiol 1988, V26, P475 HCAPLUS
(7) Barbour, A; Science 1987, V237, P409 HCAPLUS

(8) Busch, U; J Clin Microbiol 1996, V34, P1072
HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:659148 HCAPLUS
DOCUMENT NUMBER: 131:285385
TITLE: Method, **antigen** complex and kit for diagnosing Lyme borreliosis
INVENTOR(S): Staffeldt, Schou Ole; Winther, Lars; Stender, Henrik
PATENT ASSIGNEE(S): Dako A/S, Den.
SOURCE: Eur. Pat. Appl., 23 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 949508	A1	19991013	EP 1999-610026	19990407

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: DK 1998-516 19980408

AB A diagnostic method is disclosed which utilizes an **antigen** complex comprising a carrier to which is attached a plurality of Borrelia OspC peptides and optionally other Borrelia peptides. The **antigen** complex is used for detn. of IgM antibodies against B. burgdorferi sensu lato. The **antigen** complex comprises a sufficient no. of peptides having affinity for a relevant epitope on the IgM antibody to be detected to allow the **antigen** complex to bind to the IgM antibody without being removed during the washing step. The Borrelia flagellum is another important immunodominant **antigen**. The simultaneous detn. of antibodies against Borrelia OspC and flagellum is also disclosed. The method is particularly useful for diagnosing Lyme borreliosis in the early stages. An ELISA of human serum samples used **antigen** complexes contg. biotinylated flagella biotinylated OspC peptide and streptavidin-horseradish peroxidase conjugate.

IT **246219-51-2P 246219-52-3P**
RL: ARG (Analytical reagent use); DEV (Device component use); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence, as Borrelia OspC peptide in **antigen** complex; method and **antigen** complex and kit for diagnosing Lyme borreliosis)

REFERENCE COUNT: 2
REFERENCE(S): (1) Hansen, K; JOURNAL OF CLINICAL MICROBIOLOGY 1991, V29(1), P166 MEDLINE
(2) Seruminstitut, S; WO 9742221 A 1997 HCAPLUS

L4 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:804175 HCAPLUS
DOCUMENT NUMBER: 128:85027
TITLE: Genomic sequence of a Lyme disease spirochaete, Borrelia burgdorferi
AUTHOR(S): Fraser, Claire M.; Casjens, Sherwood; Huang, Wai Mun; Sutton, Granger G.; Clayton, Rebecca; Lathigra, Raju; White, Owen; Ketchum, Karen A.; Dodson, Robert; Hickey, Erin K.; Gwinn, Michelle; Dougherty, Brian; Tomb, Jean-Francois; Fleischmann, Robert D.; Richardson, Delwood; Peterson, Jeremy; Kerlavage, Anthony R.; Quackenbush, John; Salzberg, Steven;

Hanson, Mark; van Vugt, Rene; Palmer, Nanette; Adams, Mark D.; Gocayne, Jeannine; Weidman, Janice; Utterback, Teresa; Watthey, Larry; McDonald, Lisa; Artiach, Patricia; Bowman, Cheryl; Garland, Stacey; Fujii, Claire; Cotton, Matthew D.; Horst, Kurt; Roberts, Kevin; Hatch, Bonnie; Smith, Hamilton O.; Venter, J. Craig

CORPORATE SOURCE: Inst. Genomic Research, Rockville, MD, 20850, USA
SOURCE: Nature (London) (1997), 390(6660), 580-586
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Macmillan Magazines
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The genome of the bacterium Borrelia burgdorferi B31, the etiol. agent of Lyme disease, contains a linear chromosome of 910,725 base pairs and at least 17 linear and circular plasmids with a combined size of more than 533,000 base pairs. The chromosome contains 853 genes encoding a basic set of proteins for DNA replication, transcription, translation, solute transport and energy metab., but, like Mycoplasma genitalium, it contains no genes for cellular biosynthetic reactions. Because B. burgdorferi and M. genitalium are distantly related eubacteria, we suggest that their limited metabolic capacities reflect convergent evolution by gene loss from more metabolically competent progenitors. Of 430 genes on 11 plasmids, most have no known biol. function; 39% of plasmid genes are paralogs that form 47 gene families. The biol. significance of the multiple plasmid-encoded genes is not clear, although they may be involved in **antigenic** variation or immune evasion.

IT **148847-97-6**, Protein (Borrelia burgdorferi strain ATCC 35210 clone pUC-B31/ospCL+ gene ospC precursor reduced)
RL: PRP (Properties)
(amino acid sequence; genomic sequence of a Lyme disease spirochaete, Borrelia burgdorferi)

L4 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:806461 HCAPLUS
DOCUMENT NUMBER: 123:220266
TITLE: Diagnosis of early Lyme disease by assay of the OspC protein or the gene
INVENTOR(S): Padula, Steven J.
PATENT ASSIGNEE(S): University of Connecticut, USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514781	A2	19950601	WO 1994-US13540	19941122
WO 9514781	A3	19950622		
W: AU, CA, JP, RU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5620862	A	19970415	US 1993-158353	19931124
CA 2177356	AA	19950601	CA 1994-2177356	19941122
AU 9511864	A1	19950613	AU 1995-11864	19941122
PRIORITY APPLN. INFO.:			US 1993-158353	19931124
			WO 1994-US13540	19941122

AB The Borrelia burgdorferi sensu stricto outer surface protein C and the gene encoding are used in the early diagnosis of Lyme disease. Purified and recombinant forms of a 23 kDa protein from a Connecticut isolate of B. burgdorferi are described. The 23kDa protein, referred to as p23 or OspC, can be used for immunodiagnostic assays for detection of early Lyme

disease. The protein and the gene can be used to prevent Lyme disease and to diagnose or detect B. burgdorferi in human or animal tissues or body fluids. Antibodies specific for the protein can also be generated and the protein may be used as an **antigen** in vaccines (no data). Clin. studies of diagnostic immunoassays are reported.

IT **146990-46-7**, Protein pC (Borrelia burgdorferi strain PKo gene pc precursor reduced) **148847-97-6**, Protein (Borrelia burgdorferi strain ATCC 35210 clone pUC-B31/ospCL+ gene ospC precursor reduced)
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; diagnosis of early Lyme disease by assay of OspC protein or gene)

L4 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:758781 HCAPLUS
DOCUMENT NUMBER: 123:283622
TITLE: Fusion proteins of **antigenic** polypeptides of Borrelia for diagnostic and therapeutic use and their manufacture
INVENTOR(S): Dunn, John J.; Luft, Benjamin J.
PATENT ASSIGNEE(S): Associated Universities, Inc., USA
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9512676	A1	19950511	WO 1994-US12352	19941027
W: AU, CA, FI, JP, NO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6248562	B1	20010619	US 1994-235836	19940429
AU 9481274	A1	19950523	AU 1994-81274	19941027
EP 726955	A1	19960821	EP 1995-900453	19941027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.:
US 1993-148191 A 19931101
US 1994-235836 A 19940429
WO 1994-US12352 W 19941027

AB Chimeric genes for fusion proteins of at least two **antigenic** polypeptides from one or more species of Borrelia are described for manuf. of the **antigens** for vaccines against borreliosis. The proteins are also useful as immunodiagnostic reagents. The **antigenic** peptides may be from the same or different larger proteins and may be from different species. The outer surface protein OspA was purified and **antigenic** domains mapped with monoclonal antibodies. A immunol. important hypervariable region of OspA was identified. The cloning of genes for a no. of outer surface proteins and their use in the construction of chimeric genes is described.

IT **167360-66-9 167360-68-1 167360-70-5 167360-72-7**
RL: BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(amino acid sequence; fusion proteins of **antigenic** polypeptides of Borrelia for diagnostic and therapeutic use and their manuf.)

IT **167360-88-5P 167360-90-9P 167361-02-6P**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; fusion proteins of **antigenic** polypeptides of Borrelia for diagnostic and therapeutic use and their manuf.)

L4 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:397240 HCAPLUS
DOCUMENT NUMBER: 122:185342
TITLE: Immunogenic formulation of OspC **antigen** vaccines for the prevention and treatment of Lyme disease and recombinant methods for the preparation of such **antigens**
INVENTOR(S): Livey, Ian; Crowe, Brian; Dorner, Friedrich
PATENT ASSIGNEE(S): Immuno AG, Austria
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9425596	A2	19941110	WO 1994-EP1365	19940429
WO 9425596	A3	19941222		
W: AT, AU, CA, CZ, FI, HU, JP, NO, PL, RU, SI, SK, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9467229	A1	19941121	AU 1994-67229	19940429
AU 683260	B2	19971106		
EP 701612	A1	19960320	EP 1994-915562	19940429
EP 701612	B1	19980121		
R: AT, BE, CH, DE, DK, ES, FR, GB, IE, IT, LI, NL, PT, SE				
HU 72923	A2	19960628	HU 1995-2002	19940429
HU 217024	B	19991129		
JP 08509371	T2	19961008	JP 1994-523899	19940429
AT 162550	E	19980215	AT 1994-915562	19940429
ES 2114687	T3	19980601	ES 1994-915562	19940429
SK 279968	B6	19990611	SK 1995-1341	19940429
PL 178775	B1	20000630	PL 1994-311301	19940429
FI 9505150	A	19951228	FI 1995-5150	19951027
NO 9504318	A	19951229	NO 1995-4318	19951027

PRIORITY APPLN. INFO.: US 1993-53863 A 19930429
WO 1994-EP1365 W 19940429

AB Immunogenic formulations for protection against Lyme disease, use of the formulations for vaccination, OspC **antigens**, and a method for manuf. of OspC **antigens** with recombinant cells are claimed. An approach to Borrelia vaccine formulation taking into account serol., genotypic and epidemiol. information by which OspC proteins from different strains of B. burgdorferi are grouped together is described. OspC **antigens** are chosen in order to constitute a representative sample of such groupings, so that the resulting vaccine provides the greatest cross-protectivity with the fewest no. of **antigens**. Common membrane **antigen** type typing of B. burgdorferi strains, development of an OspC serovar typing scheme, RFLP anal. of ospC heterogeneity, and PCR amplification and sequencing of different alleles of the ospC gene and cluster anal. of the deduced amino acid sequences was described. Addnl., epitope mapping of anti-OspC monoclonal antibodies, cross-protection studies in gerbils, and frequency of occurrence geog. distribution of various families of OspC protein assocd. with human disease were presented. OspC **antigens** were produced with recombinant Pichia pastoris.

IT **146990-47-8**, Protein pC (Borrelia burgdorferi strain PKo gene pc reduced) **161630-08-6**, Protein (Borrelia strain IP2 gene ospC) **161630-11-1**, Protein (Borrelia strain 297 gene ospC) **161630-15-5**, Protein (Borrelia strain ACA1 gene ospC) **161630-16-6**, Protein (Borrelia strain H9 gene ospC) **161630-18-8**

RL: PRP (Properties)
(amino acid sequence; immunogenic formulation of OspC **antigen** vaccines for the prevention and treatment of Lyme disease and recombinant methods for the prepn. of such **antigens**)

L4 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:267636 HCAPLUS
DOCUMENT NUMBER: 120:267636
TITLE: Molecular characterization and expression of p23 (OspC) from a North American strain of Borrelia burgdorferi
AUTHOR(S): Padula, Steven J.; Sampieri, Alicia; Dias, Feliciano; Szczepanski, Andrew; Ryan, Raymond W.
CORPORATE SOURCE: Health Cent., Univ. Connecticut, Farmington, CT, 06030-1310, USA
SOURCE: Infect. Immun. (1993), 61(12), 5097-105
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors have found that sera from patients with early stages of Lyme disease contain predominant IgM reactivity to a major 23-kDa protein (p23) from Borrelia burgdorferi 2591 isolated in Connecticut. To characterize this immunodominant **antigen**, the authors cloned and sequenced p23 and found it to be 83% identical by nucleotide sequence and 75% identical by amino acid sequence to pC (recently renamed OspC), an abundantly expressed protein on the outer surface of PKo, a European strain of B. burgdorferi (B. Wilske, et al, 1993). Immunoelectron microscopy localized p23 to the outer membrane, confirming that p23 is the strain 2591 homolog of OspC. The North American strain B31, commonly used in serol. assays for Lyme disease, does not express OspC. Northern (RNA) blot anal. detected low levels of ospC mRNA in B31, and DNA sequencing of the ospC gene from B31 revealed a 54-bp deletion in the upstream regulatory region, possibly accounting for the low transcriptional activity of ospC. The ospC coding region from B31 was cloned and antibody-reactive OspC was expressed in Escherichia coli. An IgM ELISA using recombinant OspC as the target **antigen** shows promise for the serodiagnosis of early stages of Lyme disease.
IT **148847-97-6**, Protein p23 (Borrelia burgdorferi strain 2951)
RL: PRP (Properties)
(amino acid sequence of)

L4 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:510285 HCAPLUS
DOCUMENT NUMBER: 119:110285
TITLE: Genetic heterogeneity of the genes coding for the outer surface protein C (OspC) and the flagellin of Borrelia burgdorferi
AUTHOR(S): Jauris-Heipke, S.; Fuchs, R.; Motz, M.; Preac-Mursic, V.; Schwab, E.; Soutschek, E.; Will, G.; Wilske, B.
CORPORATE SOURCE: Max von Pettenkofer Inst., Munich, W-8000/2, Germany
SOURCE: Med. Microbiol. Immunol. (1993), 182(1), 37-50
CODEN: MMIYAO; ISSN: 0300-8584
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ospC gene coding for the outer surface protein OspC and the fla gene coding for the flagellin have been investigated in three different Borrelia burgdorferi sensu lato strains. These strains (the North American strain B31 and the European strains PKo and PBi) derive from various biol. sources (Ixodes dammini, human skin and human CSF) and belong to 3 different B. burgdorferi OspA serotypes and genospecies (OspA serotype 1, B. burgdorferi sensu stricto; OspA serotype 2, group VS461 and OspA serotype 4, B. garinii, resp.). The ospC and fla genes of the resp. strains have been amplified by polymerase chain reaction, cloned in pUC8

and sequenced. The fla as well as the ospC gene were different among the 3 strains investigated. In general the fla genes are more conserved than the ospC genes. The fla genes have the same length of 1008 nucleotides coding for proteins of 336 amino acids, whereas the ospC genes differ in length. The ospC genes of strains B31, PKo, and PBi have 630, 636, and 621 nucleotides encoding proteins of 210, 212, and 207 amino acids, resp. The ospC genes exhibit sequence identities between 70% and 74% among each other; sequence identities of the fla genes are in the range 96-97%. The ospC genes could be expressed in Escherichia coli to obtain proteins with and without leader peptides. The expression of the fla gene and an internal gene fragment resulted in the complete flagellin protein and a truncated protein (amino acids 129-251). The different ospC and fla gene products were immunoreactive with monoclonal antibodies and human sera and, thus, enlarge the spectrum of recombinant **antigens** to improve antibody detection in patients with Lyme borreliosis.

IT **148847-97-6**, Protein C (Borrelia burgdorferi strain B31 pUC-B31/ospCL+ gene ospC precursor) **148847-98-7**, Protein C (Borrelia burgdorferi strain PBi pUC-PBi/ospCL+ gene ospC precursor)
RL: PRP (Properties)
(amino acid sequence and immunoreactivity of)

L4 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:186033 HCAPLUS
DOCUMENT NUMBER: 118:186033
TITLE: Molecular analysis and expression of a Borrelia burgdorferi gene encoding a 22kDa protein (pC) in Escherichia coli
AUTHOR(S): Fuchs, R.; Jauris, S.; Lottspeich, F.; Preac-Mursic, V.; Wilske, B.; Soutschek, E.
CORPORATE SOURCE: Max von Pettenkofer-Inst., Univ. Munich, Munich, 8000/2, Germany
SOURCE: Mol. Microbiol. (1992), 6(4), 503-9
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors describe the cloning and expression of the pc gene which encodes a major immunodominant protein of B. burgdorferi, the causative agent of Lyme borreliosis. The pC protein was purified from lysates of B. burgdorferi strain PKo. After tryptic digestion of the pC protein the resulting oligopeptides were applied to a gas-phase sequenator to obtain partial amino acid sequences. The deduced oligonucleotides were used as hybridization probes. After Southern blotting, a reactive band in the 3-kb range of PstI-digested genomic DNA was detected. The insertion of these fragments into pUC vectors finally resulted in pc-pos. E. coli clones. The gene (encoding a protein with 212 amino acids) was expressed in E. coli with varying deletions at the 5' end. A sequence comparison with other outer membrane proteins of B. burgdorferi indicates processing of pC that is similar to that of lipoproteins.

IT **146990-46-7**
RL: PRP (Properties)
(amino acid sequence of, complete)

L4 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:82044 HCAPLUS
DOCUMENT NUMBER: 116:82044
TITLE: Immunologically active proteins from Borrelia burgdorferi, related test kits, vaccines, and monoclonal antibodies
INVENTOR(S): Fuchs, Renate; Wilske, Bettina; Preac-Mursic, Vera; Motz, Manfred; Soutschek, Erwin
PATENT ASSIGNEE(S): Mikrogen Molekularbiologische Entwicklungs-G.m.b.H., Germany
SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9109870	A1	19910711	WO 1990-EP2282	19901221
W: AU, CA, FI, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
DE 3942728	C1	19910523	DE 1989-3942728	19891222
DE 4018988	A1	19911219	DE 1990-4018988	19900613
DE 4018988	C2	19990708		
AU 9170586	A1	19910724	AU 1991-70586	19901221
EP 506868	A1	19921007	EP 1991-902687	19901221
EP 506868	B1	19960717		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
US 6248538	B1	20010619	US 1994-209603	19940310

PRIORITY APPLN. INFO.:
DE 1989-3942728 A 19891222
DE 1990-4018988 A 19900613
WO 1990-EP2282 A 19901221
US 1992-862535 A1 19920619

AB Immunol. active proteins of B. burgdorferi were prepd. in microorganisms by genetic engineering. The specific DNA sequences were selected from a B. burgdorferi gene bank, using suitable search methods, or represented directly by DNA amplification with selected hybridation samples and placed under the control of inducible promoters, such as the lac promoter. These proteins can be used to produce specific and sensitive diagnostic test kits. Selective combination of the immunol. active proteins makes accurate diagnosis possible. Monoclonal antibodies were produced which can be used as reagents for the detection of the bacteria directly from test samples or after cultivation. The proteins can be used to distinguish Borrelia from Treponema infections. The p41 flagellin of B. burgdorferi was cloned, sequenced, and used in an ELISA for detection of antibodies in serum.

IT **138756-96-4**, Protein pC (Borrelia burgdorferi clone pDS1PC5 22-kilodalton reduced)
RL: PROC (Process)
(amino acid sequence and mol. cloning of, for diagnosis and vaccines)

=>
=>

=> select hit rn l3 1-2
E1 THROUGH E7 ASSIGNED

=> select hit rn l4 1-12
E8 THROUGH E30 ASSIGNED

=> fil reg
FILE 'REGISTRY' ENTERED AT 18:36:38 ON 26 JUN 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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STRUCTURE FILE UPDATES: 25 JUN 2001 HIGHEST RN 343304-93-8
DICTIONARY FILE UPDATES: 25 JUN 2001 HIGHEST RN 343304-93-8

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=>
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=> d his l5

(FILE 'HCAPLUS' ENTERED AT 18:32:40 ON 26 JUN 2001)
SELECT HIT RN L3 1-2
SELECT HIT RN L4 1-12

FILE 'REGISTRY' ENTERED AT 18:36:38 ON 26 JUN 2001
L5 30 S E1-E30

=> s l5 and l1
L6 30 L5 AND L1

=> d .seq l6 1-30

L6 ANSWER 1 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **338741-11-0** REGISTRY
CN L-Glutamic acid, L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl-L-prolyl- (9CI) (CA INDEX NAME)
SQL 11
RN **338741-11-0** REGISTRY

SEQ 1 PVVAESPKKP E
==========
HITS AT: 1-10

REFERENCE 1: 134:339287

L6 ANSWER 2 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **263013-02-1** REGISTRY
CN L-Proline, N2,N6-bis(L-methionyl-L-threonyl-L-.alpha.-glutamyl-L-glutaminyl-L-glutaminyl-L-tryptophyl-L-asparaginyl-L-phenylalanyl-L-alanylglycyl-L-isoleucyl-L-.alpha.-glutamyl-L-alanyl-L-alanyl-L-alanyl-L-seryl-L-alanyl)-L-lysyl-N-(carboxymethyl)glycyl-L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl-, (19.fwdarw.1')-amide with L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl-L-proline (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 38: PN: WO0018791 PAGE: 81 claimed sequence
CN LPA-VI
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Lys-18	- Ala-17'	amide bridge
bridge	Gly-19	- Pro-1''	amide bridge

SQL 56,29,17,10
RN **263013-02-1** REGISTRY

SEQ 1 MTEQQWNFAG IEAAASAKGP VVAESPKKP
= =========
HITS AT: 20-29

```
SEQ      1 PVVAESPKKP
           ==========
HITS AT:   1-10

REFERENCE   1:  133:265384

REFERENCE   2:  132:250004

L6   ANSWER 3 OF 30  REGISTRY  COPYRIGHT 2001 ACS
RN   263013-01-0  REGISTRY
CN   L-Proline, N2,N6-bis(L-tyrosyl-L-glutaminylglycyl-L-valyl-L-glutaminyl-L-
     glutaminyl-L-lysyl-L-tryptophyl-L-.alpha.-aspartyl-L-alanyl-L-threonyl-L-
     alanyl-L-threonyl-L-.alpha.-glutamyl-L-leucyl-L-asparaginyl-L-asparaginyl-
     L-alanyl-L-leucyl-L-glutaminyl)-L-lysyl-3-aminopentanedioylbis[L-prolyl-L-
     valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl-
      (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   37: PN: WO0018791 PAGE: 81 claimed sequence
CN   LPA-V
NTE  multichain
----------------------------------------------------------------------
 type            ------ location ------         description
----------------------------------------------------------------------
bridge           Lys-21      - Gln-20'     amide bridge
bridge           Oaa-22      - Pro-1''     amide bridge
uncommon         Oaa-22          -         -
----------------------------------------------------------------------
SQL  62,32,20,10
RN   263013-01-0  REGISTRY

SEQ      1 YQGVQQKWDA TATELNNALQ KXPVVAESPK KP
                                   ======== ==
HITS AT:   23-32


SEQ      1 PVVAESPKKP
           ==========
HITS AT:   1-10

REFERENCE   1:  133:265384

REFERENCE   2:  132:250004

L6   ANSWER 4 OF 30  REGISTRY  COPYRIGHT 2001 ACS
RN   262859-59-6  REGISTRY
CN   L-Proline, L-lysyl-3-aminopentanedioylbis[L-prolyl-L-valyl-L-valyl-L-
     alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl- (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   36: PN: WO0018791 PAGE: 80 claimed sequence
CN   LPA-IV
NTE  multichain
     modified (modifications unspecified)
----------------------------------------------------------------------
 type            ------ location ------         description
----------------------------------------------------------------------
bridge           Pro-1       - Pro-1'      covalent bridge, dimer
----------------------------------------------------------------------
SQL  20,10,10
RN   262859-59-6  REGISTRY

SEQ      1 PVVAESPKKP
           ==========
```

HITS AT: 1-10

SEQ 1 PVVAESPKKP
==========
HITS AT: 1-10

REFERENCE 1: 133:265384

REFERENCE 2: 132:250004

L6 ANSWER 5 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **262859-58-5** REGISTRY
CN L-Proline, 1,1'-(3-amino-1,5-dioxo-1,5-pentanediyl)bis[L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 35: PN: WO0018791 PAGE: 80 claimed sequence
CN LPA-III
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Pro-1	- Pro-1'	covalent bridge, dimer

SQL 20,10,10
RN **262859-58-5** REGISTRY

SEQ 1 PVVAESPKKP
==========
HITS AT: 1-10

SEQ 1 PVVAESPKKP
==========
HITS AT: 1-10

REFERENCE 1: 133:265384

REFERENCE 2: 132:250004

L6 ANSWER 6 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **262859-57-4** REGISTRY
CN L-Proline, N-(carboxymethyl)-N-[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxohexyl]glycyl-L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl-, (1.fwdarw.1')-amide with L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl-L-proline (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 34: PN: WO0018791 PAGE: 80 claimed sequence
CN LPA-II
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Gly-1	- Pro-1'	covalent bridge

SQL 21,11,10
RN **262859-57-4** REGISTRY

SEQ 1 GPVVAESPKK P
========= =

HITS AT: 2-11

SEQ 1 PVVAESPKKP
==========
HITS AT: 1-10

REFERENCE 1: 133:265384

REFERENCE 2: 132:250004

L6 ANSWER 7 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **262859-56-3** REGISTRY
CN L-Proline, N-(carboxymethyl)-N-[(9H-fluoren-9-ylmethoxy)carbonyl]glycyl-L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl-, (1.fwdarw.1')-amide with L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl-L-proline (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 33: PN: WO0018791 PAGE: 79 claimed sequence
CN LPA-I
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Gly-1	- Pro-1'	covalent bridge

SQL 21,11,10
RN **262859-56-3** REGISTRY

SEQ 1 GPVVAESPKK P
========= =
HITS AT: 2-11

SEQ 1 PVVAESPKKP
==========
HITS AT: 1-10

REFERENCE 1: 133:265384

REFERENCE 2: 132:250004

L6 ANSWER 8 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **257289-49-9** REGISTRY
CN L-Proline, L-lysyl-L-threonyl-L-histidyl-L-asparaginyl-L-threonyl-L-lysyl-L-.alpha.-aspartyl-L-lysylglycyl-L-alanyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-leucyl-L-valyl-L-lysyl-L-leucyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-valyl-L-alanylglycyl-L-leucyl-L-leucyl-L-lysyl-L-valyl-L-alanyl-L-glutaminyl-L-.alpha.-glutamyl-L-threonyl-L-leucyl-L-asparaginyl-L-asparaginyl-L-seryl-L-valyl-L-lysyl-L-.alpha.-glutamyl-L-leucyl-L-threonyl-L-seryl-L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 95: PN: WO0005378 SEQID: 1 claimed protein
SQL 50
RN **257289-49-9** REGISTRY

SEQ 1 KTHNTKDKGA EELVKLAESV AGLLKVAQET LNNSVKELTS PVVAESPKKP
==========
HITS AT: 41-50

REFERENCE 1: 132:150602

L6 ANSWER 9 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **257260-46-1** REGISTRY
CN Protein (Borrelia burgdorferi strain S-1-10 gene OspC 194-amino acid fragment) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 92: PN: WO0005378 SEQID: 2 claimed protein
SQL 194
RN **257260-46-1** REGISTRY

SEQ 151 DKGAEELVKL AESVAGLLKV AQETLNNSVK ELTSPVVAES PKKP
====== ====
HITS AT: 185-194

REFERENCE 1: 132:150602

L6 ANSWER 10 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **246219-52-3** REGISTRY
CN L-Proline, L-cysteinyl-L-glutaminyl-L-valyl-L-alanyl-L-leucyl-L-threonyl-L-asparaginyl-L-seryl-L-valyl-L-lysyl-L-.alpha.-glutamyl-L-leucyl-L-threonyl-L-seryl-L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl- (9CI) (CA INDEX NAME)
SQL 24
RN **246219-52-3** REGISTRY

SEQ 1 CQVALTNSVK ELTSPVVAES PKKP
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HITS AT: 15-24

REFERENCE 1: 131:285385

L6 ANSWER 11 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **246219-51-2** REGISTRY
CN L-Proline, N2-[[2-[2-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]ethoxy]ethoxy]acetyl]-L-glutaminyl-L-valyl-L-alanyl-L-leucyl-L-threonyl-L-asparaginyl-L-seryl-L-valyl-L-lysyl-L-.alpha.-glutamyl-L-leucyl-L-threonyl-L-seryl-L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl- (9CI) (CA INDEX NAME)
NTE modified

type	------ location ------		description
modification	Gln-1	-	undetermined modification

SQL 23
RN **246219-51-2** REGISTRY

SEQ 1 QVALTNSVKE LTSPVVAESP KKP
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HITS AT: 14-23

REFERENCE 1: 131:285385

L6 ANSWER 12 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **199437-17-7** REGISTRY
CN L-Proline, L-prolyl-L-valyl-L-valyl-L-alanyl-L-.alpha.-glutamyl-L-seryl-L-prolyl-L-lysyl-L-lysyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1: PN: WO0018791 SEQID: 1 claimed protein
SQL 10
RN **199437-17-7** REGISTRY

SEQ 1 PVVAESPKKP

```
          ==========
HITS AT:  1-10

REFERENCE   1:  132:250004

REFERENCE   2:  130:181185

REFERENCE   3:  129:288851

REFERENCE   4:  128:21860

L6   ANSWER 13 OF 30  REGISTRY  COPYRIGHT 2001 ACS
RN   169539-68-8  REGISTRY
CN   Protein (Borrelia garinii strain PTrob gene ospC outer surface) (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   GenBank AJ236908-derived protein GI 5326934
CN   Lipoprotein (Borrelia garinii strain Pscf gene ospC)
CN   Outer surface protein C (Borrelia garinii strain Pscf gene ospC)
SQL  207
RN   169539-68-8  REGISTRY

SEQ    151 NAKKAILKTH GTKDKGAKEL EELFKSLESL SKAAQAALTN SVKELTNPVV
                                                          ===
       201 AESPKKP
           =======
HITS AT:  198-207

REFERENCE   1:  132:148850

REFERENCE   2:  124:1985

L6   ANSWER 14 OF 30  REGISTRY  COPYRIGHT 2001 ACS
RN   167361-02-6  REGISTRY
CN   Lipoprotein (Borrelia burgdorferi strain B31 gene ospB) fusion protein
     with protein p41 (Borrelia burgdorferi strain B31) fusion protein with
     protein (Borrelia burgdorferi strain B31 gene ospC) (9CI)  (CA INDEX NAME)
SQL  588
RN   167361-02-6  REGISTRY

SEQ    451 KAAKEMLANS VKELTSPVVA ESPKKPGTMA QYNQMHMLSN KSASQNVRTA
                          ==== ======
HITS AT:  467-476

REFERENCE   1:  123:283622

L6   ANSWER 15 OF 30  REGISTRY  COPYRIGHT 2001 ACS
RN   167360-90-9  REGISTRY
CN   Protein (Borrelia burgdorferi strain B31 gene ospC) fusion protein with
     lipoprotein (Borrelia burgdorferi strain B31 gene ospA) fusion protein
     with lipoprotein (Borrelia burgdorferi strain B31 gene ospB) (9CI)  (CA
     INDEX NAME)
SQL  466
RN   167360-90-9  REGISTRY

SEQ    201 PVVAESPKKP KQNVSSLDEK NSVSVDLPGE MKVLVSKEKN KDGKYDLIAT
           ==========
HITS AT:  201-210

REFERENCE   1:  123:283622

L6   ANSWER 16 OF 30  REGISTRY  COPYRIGHT 2001 ACS
RN   167360-88-5  REGISTRY
```

CN Lipoprotein (Borrelia burgdorferi strain B31 gene ospA) fusion protein with lipoprotein (Borrelia burgdorferi strain B31 gene ospB) fusion protein with protein (Borrelia burgdorferi strain B31 gene ospC) (9CI) (CA INDEX NAME)
SQL 466
RN **167360-88-5** REGISTRY

SEQ 451 VKELTSPVVA ESPKKP
==== ======
HITS AT: 457-466

REFERENCE 1: 123:283622

L6 ANSWER 17 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **167360-72-7** REGISTRY
CN Protein (Borrelia burgdorferi strain TRO gene ospC) (9CI) (CA INDEX NAME)
SQL 207
RN **167360-72-7** REGISTRY

SEQ 151 NAKKAILKTH GTKDKGAKEL EELFKSLESL SKAAQAALTN SVKELTNPVV
===
201 AESPKKP
=======
HITS AT: 198-207

REFERENCE 1: 123:283622

L6 ANSWER 18 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **167360-70-5** REGISTRY
CN Protein (Borrelia burgdorferi strain PKO gene ospC) (9CI) (CA INDEX NAME)
SQL 212
RN **167360-70-5** REGISTRY

SEQ 201 TSPVVAESPK KP
======== ==
HITS AT: 203-212

REFERENCE 1: 123:283622

L6 ANSWER 19 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **167360-68-1** REGISTRY
CN Protein (Borrelia burgdorferi strain K48 gene ospC) (9CI) (CA INDEX NAME)
SQL 209
RN **167360-68-1** REGISTRY

SEQ 151 DDHAKEAILK SNPTKDKGAK ALKDLSESVE SLAKAAQEAL ANSVKELTNP
=
201 VVAESPKKP
=========
HITS AT: 200-209

REFERENCE 1: 123:283622

L6 ANSWER 20 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **167360-66-9** REGISTRY
CN Protein (Borrelia burgdorferi strain B31 gene ospC) (9CI) (CA INDEX NAME)
SQL 210
RN **167360-66-9** REGISTRY

SEQ 201 PVVAESPKKP
==========
HITS AT: 201-210

REFERENCE 1: 123:283622

L6 ANSWER 21 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **161630-18-8** REGISTRY
CN Protein (Borrelia strain VS461 gene ospC) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Antigen (Borrelia strain VS461 gene ospC)
SQL 191
RN **161630-18-8** REGISTRY

SEQ 151 AKELEELFKS VESLSKAAKE ALSNSVKELT SPVVAESPKK P
========== =
HITS AT: 182-191

REFERENCE 1: 122:185342

L6 ANSWER 22 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **161630-16-6** REGISTRY
CN Protein (Borrelia strain H9 gene ospC) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Antigen (Borrelia strain H9 gene ospC)
CN Protein (Borrelia afzelii strain H9 gene ospC reduced)
SQL 194
RN **161630-16-6** REGISTRY

SEQ 151 DKGAEELEKL FKSVESLAKA AKESLTNSVK ELTNPVVAES PKKP
====== ====
HITS AT: 185-194

REFERENCE 1: 124:78452

REFERENCE 2: 122:185342

L6 ANSWER 23 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **161630-15-5** REGISTRY
CN Protein (Borrelia strain ACA1 gene ospC) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Antigen (Borrelia strain ACA1 gene ospC)
CN Protein (Borrelia afzelii strain ACA1 gene ospC reduced)
SQL 193
RN **161630-15-5** REGISTRY

SEQ 151 KGAEELGKLF KSVEGLVKAA QEALTNSVKE LTSPVVAESP KKP
======= ===
HITS AT: 184-193

REFERENCE 1: 124:78452

REFERENCE 2: 122:185342

L6 ANSWER 24 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **161630-11-1** REGISTRY
CN Protein (Borrelia strain 297 gene ospC) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Antigen (Borrelia strain 297 gene ospC)
CN Protein (Borrelia burgdorferi sensu stricto strain 297 gene ospC reduced)
SQL 192
RN **161630-11-1** REGISTRY

SEQ 151 GADELEKLFE SVKNLSKAAK EMLTNSVKEL TSPVVAESPK KP
======== ==
HITS AT: 183-192

REFERENCE 1: 124:78452

REFERENCE 2: 122:185342

L6 ANSWER 25 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **161630-08-6** REGISTRY
CN Protein (Borrelia strain IP2 gene ospC) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Antigen (Borrelia strain IP2 gene ospC)
CN Protein (Borrelia burgdorferi sensu stricto strain IP2 gene ospC reduced)
SQL 192
RN **161630-08-6** REGISTRY

SEQ 151 GAEELGKLFE SVEVLSKAAK EMLANSVKEL TSPVVAESPK KP
========= ==
HITS AT: 183-192

REFERENCE 1: 124:78452

REFERENCE 2: 122:185342

L6 ANSWER 26 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **148847-98-7** REGISTRY
CN Protein (Borrelia burgdorferi strain PBi clone pUC-PBi/ospCL+ gene ospC precursor reduced) (9CI) (CA INDEX NAME)
SQL 207
RN **148847-98-7** REGISTRY

SEQ 151 NAKKAILKTH GTKDKGAKEL EELFKSLESL SKAAQAALTN SVKELTNPVV
===
201 AESPKKP
=======
HITS AT: 198-207

REFERENCE 1: 119:110285

L6 ANSWER 27 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **148847-97-6** REGISTRY
CN Protein (Borrelia burgdorferi strain ATCC 35210 clone pUC-B31/ospCL+ gene ospC precursor reduced) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN GenBank AE000792-derived protein GI 2689901
CN Outer surface protein (Borrelia burgdorferi gene ospC)
CN Outer surface protein C (ospC) (Borrelia burgdorferi strain B31 gene BBB19)
CN Protein (Borrelia burgdorferi strain ATCC 35210 gene ospC reduced)
SQL 210
RN **148847-97-6** REGISTRY

SEQ 201 PVVAESPKKP
==========
HITS AT: 201-210

REFERENCE 1: 128:85027

REFERENCE 2: 124:2205

REFERENCE 3: 123:220266

REFERENCE 4: 120:267636

REFERENCE 5: 119:110285

L6 ANSWER 28 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **146990-47-8** REGISTRY
CN Protein pC (Borrelia burgdorferi strain PKo gene pc reduced) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Antigen (Borrelia strain JS3 gene ospC)
CN Protein (Borrelia afzelii strain JSB gene ospC reduced)
CN Protein (Borrelia strain JS3 gene ospC)
SQL 194
RN **146990-47-8** REGISTRY

SEQ 151 DKGAKEFKDL FESVEGLLKA AQVALTNSVK ELTSPVVAES PKKP
====== ====
HITS AT: 185-194

REFERENCE 1: 124:78452

REFERENCE 2: 122:185342

L6 ANSWER 29 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **146990-46-7** REGISTRY
CN Protein pC (Borrelia burgdorferi strain PKo gene pc precursor reduced) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Outer surface protein (Borrelia burgdorferi gene ospC)
SQL 212
RN **146990-46-7** REGISTRY

SEQ 201 TSPVVAESPK KP
======== ==
HITS AT: 203-212

REFERENCE 1: 123:220266

REFERENCE 2: 118:186033

L6 ANSWER 30 OF 30 REGISTRY COPYRIGHT 2001 ACS
RN **138756-96-4** REGISTRY
CN Protein pC (Borrelia burgdorferi clone pDS1PC5 22-kilodalton reduced) (9CI) (CA INDEX NAME)
SQL 212
RN **138756-96-4** REGISTRY

SEQ 201 TSPVVAESPK KP
======== ==
HITS AT: 203-212

REFERENCE 1: 116:82044

```
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                 ARD SOREN"/AU OR "OSTERGAARD SOREN"/IN)


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L10  ANSWER 1 OF 19  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:        2000:844273  HCAPLUS
DOCUMENT NUMBER:         134:129026
TITLE:                   Short communication: associations between blood
                         calcium status at calving and milk yield in dairy cows
AUTHOR(S):               Ostergaard, S.; Larsen, T.
CORPORATE SOURCE:        Dep. Anim. Health Welfare, Res. Cent. Foulum, Dan.
                         Inst. Agric. Sci., Tjele, DK-8830, Den.
SOURCE:                  J. Dairy Sci. (2000), 83(11), 2438-2440
                         CODEN: JDSCAE; ISSN: 0022-0302
PUBLISHER:               American Dairy Science Association
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   The purpose of the present study was to est. the effect of total blood
     plasma calcium (TBPCC) concn. at calving on milk yield in dairy cows.
     Data originated from 153 dairy cows in 27 herds from a single veterinary
     practice.  For each cow, data included calcium concn. in a blood sample
     taken within 12 h postpartum, monthly test-day milk yield until 300 days
     in milk, calving date, parity, breed, and herd.  The TBPCC ranged from
     0.69 to 2.73 mmol/L, with a mean value of 1.80 mmol/L.  The statistical
     anal. adjusted for the fixed effects of parity and lactation stage, random
     effects of herd and cow, and the correlation between repeated measures of
     test-day milk yield.  TBPCC at calving was not significantly related to
     fat- and protein-cor. milk yield at any lactation period.  Hypocalcemia
```

(low TBPCC) at calving is not an important risk factor for decreased milk yield.
REFERENCE COUNT: 15
REFERENCE(S): (4) Gitelman, H; Anal Biochem 1967, V18, P521 HCAPLUS
(5) Horst, R; J Dairy Sci 1997, V80, P1269 HCAPLUS
(11) Ostergaard, S; J Dairy Sci 1999, V82, P1188 HCAPLUS
(12) Ostergaard, S; J Dairy Sci 2000, V83, P721 HCAPLUS
(14) Rajala-Schultz, P; J Dairy Sci 1999, V82, P288 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:569091 HCAPLUS
DOCUMENT NUMBER: 133:265384
TITLE: Ligand-presenting assembly: a method for C- and N-terminal antigen presentation
AUTHOR(S): Holm, A.; Jorgensen, R. M.; **Ostergaard, S.**; Theisen, M.
CORPORATE SOURCE: Research Center for Medical Biotechnology, Chemistry Department, The Royal Veterinary and Agricultural University, Copenhagen, DK-1871, Den.
SOURCE: J. Pept. Res. (2000), 56(2), 105-113
CODEN: JPERFA; ISSN: 1397-002X
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Achiral dicarboxylic acids were coupled with 2 equiv. of the free .alpha.-amino groups of two fully side-chain protected peptide chains while these were still attached to a synthesis resin. Cleavage from the resin with simultaneous side-chain deprotection afforded two assembled peptide chains with free C-terminals. Suitable functionalization of the achiral dicarboxylic acid alternatively permitted continued peptide synthesis in a C to N orientation leading to a final peptide assembly which, after cleavage from the resin, may have multiple N to C and C to N presentation of one or more epitopes.
REFERENCE COUNT: 16
REFERENCE(S): (1) Aletras, A; J Peptide Protein Res 1995, V45, P488 HCAPLUS
(2) Bhatnagar, P; J Med Chem 1996, V39, P3814 HCAPLUS
(3) Brandt, L; J Immunol 1996, V157, P3527 HCAPLUS
(5) Keah, H; J Peptide Res 1998, V51, P2 HCAPLUS
(6) Kim, H; J Med Chem 1994, V37, P3373 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:291651 HCAPLUS
TITLE: A stochastic model simulating the feeding-health-production complex in a dairy herd
AUTHOR(S): **Ostergaard, S.**; Sorensen, J. T.; Kristensen, A. R.
CORPORATE SOURCE: Department of Animal Science and Animal Health, Royal Veterinary and Agricultural University, Copenhagen, DK-1870, Den.
SOURCE: J. Dairy Sci. (2000), 83(4), 721-733
CODEN: JDSCAE; ISSN: 0022-0302
PUBLISHER: American Dairy Science Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A dynamic, stochastic, and mechanistic Monte Carlo model, simulating a dairy herd with focus on the feeding-health-prodn. complex is presented. By specifying biol. parameters at cow level and a management strategy at

herd level, the model can simulate the tech. and economic consequences of scenarios at herd level. The representation of the feeding-health-prodn. complex is aimed to be sufficiently detailed, to include relationships likely to cause significant herd effects, and to be sufficiently simple to enable a feasible parameterization of the model and interpretation of the results from the model. Consequently, diseases are defined as four disease types: two metabolic disease types, an udder disease type, and a reproductive disease type. Risk factors for the diseases were defined as parity, yield capacity, disease recurrence, disease interrelationships, lactation stage, and season. Direct effects of the diseases were defined according to milk yield, feed intake, feed utilization, conception, culling, involuntary removal, and death. Scenarios differing in base risks of milk fever and ketosis, heat detection rate, and culling strategy were simulated for describing the model behavior. Annual milk yield per cow was decreased by increased risk of ketosis and by increased risk of milk fever, even though no direct effect of milk fever on milk yield was modeled at the cow level. The indirect effect from milk fever is a consequence of increased replacement rate (relatively lower milk yield from younger cows). By ignoring the history of milk fever in insemination and replacement decisions, a significantly reduced net income per cow was found in some herds. We concluded that important benefits from using such a herd model are the capability of accounting for herd management factors and the advantage of avoiding to double count the indirect effects from disease, such as increased risk of other diseases, poorer reprodn. results, and increased risk of culling and death.

REFERENCE COUNT: 43
REFERENCE(S):
(4) Detilleux, J; J Dairy Sci 1994, V77, P3316 HCAPLUS
(18) Grohn, Y; J Dairy Sci 1995, V78, P1693 HCAPLUS
(19) Grohn, Y; J Dairy Sci 1998, V81, P966 HCAPLUS
(22) Heuer, C; J Dairy Sci 1999, V82, P295 HCAPLUS
(31) Ostergaard, S; J Dairy Sci 1999, V82, P1188 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:288716 HCAPLUS
DOCUMENT NUMBER: 133:135599
TITLE: Complex and diverse motif bead libraries based on the peptomer (peptide/peptoid hybrid polymer) approach
AUTHOR(S): **Ostergaard, Soren**; Hansen, Per Hertz
CORPORATE SOURCE: Novo Nordisk A/S, Bagsvaerd, 2880, Den.
SOURCE: Pept. 1998, Proc. Eur. Pept. Symp., 25th (1999), Meeting Date 1998, 758-759. Editor(s): Bajusz, Sandor; Hudecz, Ferenc. Akademiai Kiado: Budapest, Hung.
CODEN: 68WKAY
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. TentaGel resin-bound peptide libraries (contg. peptide/peptoid hybrid polymers) were synthesized and screened against streptavidin alk. phosphatase under low and high stringency conditions.
REFERENCE COUNT: 3
REFERENCE(S):
(1) stergaard, S; J Peptide Sci 1997, V3, P123
(2) stergaard, S; Mol Div 1997, V3, P17
(3) Zuckermann, R; J Am Chem Soc 1992, V114, P10646 HCAPLUS

L10 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:227686 HCAPLUS
DOCUMENT NUMBER: 132:284221
TITLE: NCAM-binding compounds for stimulation of nerve outgrowth and proliferation of NCAM-presenting cells
INVENTOR(S): Ronn, Lars Christian B.; Bock, Elisabeth; Holm, Arne;

Olsen, Marianne; **Ostergaard, Soren**; Jensen, Peter H.; Poulsen, Flemming M.; Soroka, Vladislav; Ralets, Igor; Berezin, Vladimir
PATENT ASSIGNEE(S): Den.
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018801	A2	20000406	WO 1999-DK500	19990923
WO 2000018801	A3	20000713		

W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9957274	A1	20000417	AU 1999-57274	19990923

PRIORITY APPLN. INFO.:

DK 1998-1232	A	19980929
DK 1999-592	A	19990429
WO 1999-DK500	W	19990923

OTHER SOURCE(S): MARPAT 132:284221
AB The invention provides novel compds. which are able to stimulate proliferation or/and outgrowth from cells presenting the neural cell adhesion mol. (NCAM). Addnl., the invention relates to pharmaceutical compns., medicaments and methods for treatment of normal, degenerated and damaged NCAM-presenting cells.

L10 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:227676 HCAPLUS
DOCUMENT NUMBER: 132:250004
TITLE: Ligand presenting assembly (LPA), method of preparation and uses thereof
INVENTOR(S): Holm, Arne; Jorgensen, Rikke Malene; **Ostergaard, Soren**; Theisen, Michael
PATENT ASSIGNEE(S): Statens Serum Institut, Den.
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000018791	A1	20000406	WO 1999-DK510	19990929

W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9960783	A1	20000417	AU 1999-60783	19990929

PRIORITY APPLN. INFO.: DK 1998-1233 A 19980929
WO 1999-DK510 W 19990929
OTHER SOURCE(S): MARPAT 132:250004
AB The present invention relates to a method for prepg. a Ligand Presenting Assembly (LPA), an LPA, an immunol. compn. and a vaccine. The N-terminal of LPA is coupled to an achiral di, tri, or tetra-carboxylic acid so as to provide a construct having a ring structure. The invention further relates to a method for generating antibodies, a kit for use in diagnosis and use of an LPA for prepg. a pharmaceutical compn.
REFERENCE COUNT: 7
REFERENCE(S): (1) Anthony, G; WO 9402506 A 1994 HCAPLUS
(2) Golding Louise; WO 9832469 A 1998 HCAPLUS
(3) Harboe, M; INFECTION AND IMMUNITY 1998, V66(2), P717 HCAPLUS
(4) Peluso, S; TETRAHEDRON 1997, V53(21), P7231 HCAPLUS
(5) Statens Seruminstitut; WO 9742221 A 1997 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:34958 HCAPLUS
DOCUMENT NUMBER: 132:88169
TITLE: Peptide antagonists of the human urokinase plasminogen activator receptor, selection method, and therapeutic use, especially for the treatment of cancer
INVENTOR(S): Ploug, Michael; **Ostergaard, Soren**; Holm, Arne; Holst-Hansen, Claus; Stephens, Ross W.; Dano, Keld
PATENT ASSIGNEE(S): Cancerforskningsfonden Af 1989 (Fonden Til Fremme Af Eksperimentel Cancerforskning, Den.
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000001802	A2	20000113	WO 1999-DK377	19990701
WO 2000001802	A3	20000427		
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9947688	A1	20000124	AU 1999-47688	19990701

PRIORITY APPLN. INFO.: DK 1998-874 A 19980701
WO 1999-DK377 W 19990701
AB A set of inhibitors of the binding interaction between human urokinase plasminogen activator (uPA) and its cell surface receptor (uPAR) has been developed. The inhibitors comprise peptide fragments, monomeric or in multiple copies attached to a common scaffold, in which the amino acid sequence may include uncommon substituted amino acids to partially comprise of peptoid sequences. The invention also relates to the use of such peptides in therapy, in particular for the treatment of cancer, having developed a modified non-human mammalian receptor to which the novel inhibitors are antagonistic.

L10 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:683626 HCAPLUS
DOCUMENT NUMBER: 131:349587
TITLE: Identification of a neuritogenic ligand of the neural cell adhesion molecule using a combinatorial library of synthetic peptides
AUTHOR(S): Ronn, Lars C. B.; Olsen, Marianne; **Ostergaard, Soren**; Kiselyov, Vladislav; Berezin, Vladimir; Mortensen, Marie T.; Lerche, Mathilde H.; Jensen, Peter H.; Soroka, Vladislav; Saffells, Jane L.; Doherty, Patrick; Poulsen, Flemming M.; Bock, Elisabeth; Holm, Arne
CORPORATE SOURCE: Protein Lab., Inst. Mol. Pathol., Panum Inst. 6.2, Univ. Copenhagen, Copenhagen N, DK-2200, Den.
SOURCE: Nat. Biotechnol. (1999), 17(10), 1000-1005
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The neural cell adhesion mol. (NCAM) plays a key role in neural development, regeneration, and learning. In this study, we identified a synthetic peptide-ligand of the NCAM Ig1 module by combinatorial chem. and showed it could modulate NCAM-mediated cell adhesion and signal transduction with high potency. In cultures of dissocd. neurons, this peptide, termed C3, stimulated neurite outgrowth by activating a signaling pathway identical to that activated by homophilic NCAM binding. A similar effect was shown for the NCAM Ig2 module, the endogenous ligand of NCAM Ig1. By NMR spectroscopy, the C3 binding site in the NCAM Ig1 module was mapped and shown to be different from the binding site of the NCAM Ig2 module. The C3 peptide may prove useful as a lead in development of therapies for neurodegenerative disorders, and the C3 binding site of NCAM Ig1 may represent a target for discovery of nonpeptide drugs.
REFERENCE COUNT: 41
REFERENCE(S): (1) Beggs, H; J Biol Chem 1997, V272, P8310 HCAPLUS
(2) Bothner-By, A; J Am Chem Soc 1984, V106, P811 HCAPLUS
(4) Covault, J; Proc Natl Acad Sci USA 1985, V82, P4544 HCAPLUS
(5) Cremer, H; Nature 1994, V367, P455 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:399862 HCAPLUS
TITLE: Effects of diseases on test day milk yield and body weight of dairy cows from Danish research herds
AUTHOR(S): **Ostergaard, S.**; Grohn, Y. T.
CORPORATE SOURCE: Department of Animal Science and Animal Health, Royal Veterinary and Agricultural University, Copenhagen, DK-1870, Den.
SOURCE: J. Dairy Sci. (1999), 82(6), 1188-1201
CODEN: JDSCAE; ISSN: 0022-0302
PUBLISHER: American Dairy Science Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pre- and postdisease interrelationships of energy cor. test day milk yield and body wt. of dairy cows caused by mastitis, three reproductive disorders (retained placenta, metritis, cystic ovaries), and seven metabolic disorders (milk fever, ketosis, decreased rumen motility, enteritis, left displaced abomasum, right displaced abomasum, and off feed) were quantified by using mixed models anal. with repeated measures of continuous data. The data were weekly recordings from 4414 lactations collected in three Danish research herds. High milk yield was a risk

factor for ketosis and enteritis. Heavier primiparous cows were more likely to contract mastitis. Milk yield was decreased for a disease-specific period for all study diseases except cystic ovaries and right displaced abomasum. Metabolic disorders had a detrimental effect on body wt. The highest wt. loss (69 kg) was assocd. with left displaced abomasum. The persistence of the wt. loss differed considerably among study diseases. Almost all wt. loss occurred up to and including the initial week after diagnosis, which emphasized the detrimental effect of the subclin. stage. However, weekly measured body wt. seemed superior to weekly energy cor. test day milk yield for disease detection only for decreased rumen motility and left displaced abomasum. This study demonstrates the importance of the predisease level for accurate estn. of the loss of milk yield and body wt. from disease.

REFERENCE COUNT: 39

REFERENCE(S):
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(17) Grohn, Y; J Dairy Sci 1995, V78, P1693 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:38999 HCAPLUS

DOCUMENT NUMBER: 130:179184

TITLE: Identification and purification of O-acetyl-L-serine sulfhydrylase in Penicillium chrysogenum

AUTHOR(S): **Ostergaard, S.**; Theilgaard, H. B. Aa.; Nielsen, J.

CORPORATE SOURCE: Centre for Process Biotechnology, Department of Biotechnology, Technical University of Denmark, Lyngby, DK-2800, Den.

SOURCE: Appl. Microbiol. Biotechnol. (1998), 50(6), 663-668
CODEN: AMBIDG; ISSN: 0175-7598

PUBLISHER: Springer-Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors demonstrate that P. chrysogenum possesses the L-cysteine biosynthetic enzyme O-acetyl-L-serine sulfhydrylase (EC 4.2.99.8) (I) of the direct sulfhydrylation pathway. The finding of I, and thus the presence of the direct sulfhydrylation pathway in P. chrysogenum, creates the potential for increasing the overall yield in penicillin prodn. by enhancing the enzymic activity of this microorganism. Only I and O-acetyl-L-homoserine sulfhydrylase (EC 4.2.99.10) (II) have been demonstrated to use O-acetyl-L-serine as substrate for the formation of L-cysteine. Purified I did not catalyze the formation of L-homocysteine from O-acetyl-L-homoserine and sulfide, thus excluding the possibility that the purified enzyme was a II with multiple substrate specificity. I purifn. enhanced the specific activity 93-fold in relation to the cell-free ext. Two bands, showing exactly the same intensity, were present in SDS-PAGE, and the mol. wts. of these were estd. to be 59 and 68 kDa, resp. The Km and Vmax values of I with O-acetyl-L-serine as substrate were estd. as 1.3 mM and 14.9 .mu.mol/mg protein/h, resp. Purified I had a temp. optimum of .apprx.45.degree., which was much higher than the actual temp. for penicillin synthesis. Furthermore, I exhibited max. activity in the range of pH 7.0-7.4.

REFERENCE COUNT: 19

REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:574780 HCAPLUS
DOCUMENT NUMBER: 129:288851
TITLE: The dominant epitope of Borrelia garinii outer surface protein C recognized by sera from patients with neuroborreliosis has a surface-exposed conserved structural motif
AUTHOR(S): Mathiesen, Marianne J.; Holm, Arne; Christiansen, Michael; Blom, Jens; Hansen, Klaus; **Ostergaard, Soren**; Theisen, Michael
CORPORATE SOURCE: Department of Clinical Biochemistry, Statens Serum Institut, Copenhagen, DK-2300, Den.
SOURCE: Infect. Immun. (1998), 66(9), 4073-4079
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Epitope mapping of outer surface protein C (OspC) by using sera from patients with neuroborreliosis led to the identification of one single major immunodominant epitope within the C-terminal 10 amino acid residues. Peptide binding studies and alanine replacement scanning of the C-terminal decapeptide, PVVAESPKKP, revealed a crit. role for the PKKP sequence and its terminal carboxyl group for the binding of IgM (IgM) antibodies from patients with Lyme borreliosis. Electron microscopy of antibody-labeled spirochetes indicated that the C-terminal region is exposed on the surface of the spirochete. Based on homol. to proteins of known function, this region most probably adopts a polyproline II-like helix, which is found in surface-exposed structures involved in protein-protein interactions. This structural motif is highly conserved in Borrelia species causing Lyme borreliosis and subjected to purifying selection. We suggest that the abundance of the C-terminal region of OspC on the surface of B. burgdorferi allows a multimeric high-avidity interaction between the spirochete and surface Igs on B cells. The resulting crosslinking of surface Igs on B cells may induce a T-cell-independent B-cell activation without IgM-to-IgG switching, thus explaining the lack of IgG antibodies to OspC in neuroborreliosis.

L10 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:206221 HCAPLUS
DOCUMENT NUMBER: 129:3180
TITLE: Evidence against protein kinase B as a mediator of contraction-induced glucose transport and GLUT4 translocation in rat skeletal muscle
AUTHOR(S): Lund, S.; Pryor, P. R.; **Ostergaard, S.**; Schmitz, O.; Pedersen, O.; Holman, G. D.
CORPORATE SOURCE: Kommunehospitalet, Aarhus Kommunehospital and Medical Department M (Endocrinology and Diabetes), Medical Research Laboratory, Aarhus University Hospital, Aarhus, 8000, Den.
SOURCE: FEBS Lett. (1998), 425(3), 472-474
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Both insulin and muscle contraction stimulate glucose transport activity. However, contraction stimulation does not involve the insulin signaling intermediate phosphatidylinositol 3-kinase (PI 3-kinase). Protein kinase B (PKB) has recently been identified as a direct downstream target of PI 3-kinase in the insulin signaling pathway. We have examd. here whether the 2 stimuli share PKB as a convergent step in sep. signaling pathways.

Insulin stimulates both glucose transport, GLUT4 cell-surface content, and PKB activity (by 4-6-fold above basal) in a wortmannin-sensitive manner in in vitro incubated rat soleus muscles. By contrast, muscle contraction, which stimulates glucose transport and the cell surface content of GLUT4 by 3-fold above basal levels, had no effect on PKB activity. These data demonstrate that PKB is not a mediator of contraction-induced glucose transport and GLUT4 translocation.

L10 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:138306 HCAPLUS
DOCUMENT NUMBER: 128:230665
TITLE: Peptomers: a versatile approach for the preparation of diverse combinatorial peptidomimetic bead libraries
AUTHOR(S): **Ostergaard, Soren**; Holm, Arne
CORPORATE SOURCE: Novo Research Institute, Bagsvaerd, DK-2880, Den.
SOURCE: Mol. Diversity (1997), 3(1), 17-27
CODEN: MODIF4; ISSN: 1381-1991
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This report describes a versatile approach in the generation of peptidomimetic bead libraries. The method is based on the prepn. of peptide-peptoid hybrids using the portioning-mixing procedure, which gives diverse peptidomimetic bead libraries composed of peptides, peptoids and peptide-peptoid hybrids. We term these peptomers, from peptide-peptoid hybrid polymers. The synthesis of the peptomers is easily accomplished by adapting the peptoid synthesis strategy, in which a primary amine reacts with bromoacetic acid, and we combine this methodol. with conventional peptide synthesis. The sequence of the active compd. is deduced by conventional microsequencing using Edman degrdn. chem., thus avoiding the synthesis of a coding structure or the addn. of mol. tags. We demonstrate the utility of the peptomer approach by the synthesis of a bead library together with the identification of novel peptidomimetic ligands binding to the macromol. targets streptavidin and the insulin receptor.

L10 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:129640 HCAPLUS
DOCUMENT NUMBER: 128:267353
TITLE: Photoaffinity Labeling of the Human Receptor for Urokinase-Type Plasminogen Activator Using a Decapeptide Antagonist. Evidence for a Composite Ligand-Binding Site and a Short Interdomain Separation
AUTHOR(S): Ploug, Michael; **Ostergaard, Soren**; Hansen, Lars Bo Laurenborg; Holm, Arne; Dano, Keld
CORPORATE SOURCE: Finsen Laboratory, Rigshospitalet, Copenhagen, DK-2100, Den.
SOURCE: Biochemistry (1998), 37(11), 3612-3622
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Binding of urokinase-type plasminogen activator (uPA) to its cellular receptor (uPAR) renders the cell surface a favored site for plasminogen activation. Recently, a 15-mer peptide antagonist of the uPA-uPAR interaction, with an IC50 value of 10 nM, was identified using phage display technol. [Goodson, R. J., Doyle, M. V., Kaufman, S. E., and Rosenberg, S. (1994) Proc. Natl. Acad. Sci. 91, 7129-7133]. In the present study, the mol. aspects of the interaction between this peptide and uPAR have been investigated. We have characterized the real-time receptor binding kinetics for the antagonist using surface plasmon resonance and identified crit. residues by alanine replacements. The minimal peptide antagonist thus derived (SLNFSQYLWS) was rendered photoactivatable by replacing residues important for uPAR binding with

WO 1997-DK203 19970502

AB A diagnostic method is disclosed which utilizes short C-terminal fragments of Borrelia burgdorferi sensu lato derived protein OspC. A 4 N-terminal amino acid peptide (Pro-Lys-Lys-Pro) is shown to be essential in immune reactivity between sera from patients suffering from early borreliosis and various OspC derivs. and it is shown that to be effective as a diagnostic agent, 5 consecutive amino acid residues must be present. Therefore, an immunol. agent used according to the invention comprises a .gtoreq. 5 amino acid residues long homolog of a fragment identical to the 10 C-terminal amino acids of OspC. Also disclosed are vaccines utilizing the short peptides as well as methods for their prepn.

L10 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:336552 HCAPLUS
DOCUMENT NUMBER: 127:62746
TITLE: Characterization of Chlamydia trachomatis L2-induced tyrosine-phosphorylated HeLa cell proteins by two-dimensional gel electrophoresis
AUTHOR(S): Birkelund, Svend; Bini, Luca; Pallini, Vitaliano; Sanchez-Campillo, Maria; Liberatori, Sabrina; Clausen, Johannes D.; **Ostergaard, Soren**; Holm, Arne; Christiansen, Gunna
CORPORATE SOURCE: Department Medical Microbiology Immunology, University Aarhus, Aarhus, DK-8000, Den.
SOURCE: Electrophoresis (1997), 18(3-4), 563-567
CODEN: ELCTDN; ISSN: 0173-0835
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chlamydia trachomatis is an obligate intracellular bacterium, inducing its own uptake in nonprofessional phagocytes either by phagocytosis or pinocytosis. We have previously shown that C. trachomatis L2 induces tyrosine phosphorylation of eukaryotic proteins upon their entry by phagocytosis. In this paper we characterize the tyrosine-phosphorylated proteins by two-dimensional gel electrophoresis. In immunoblotting with anti-phosphotyrosine antibodies of C. trachomatis L2-infected HeLa cells, but not with uninfected cells, two rows of spots were obsd. with a mol. mass of 69 and 71 kDa and pI from 5.0 to 5.2. In addn., a single spot of 100 kDa and pI 6.2 was obsd.

L10 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:98222 HCAPLUS
DOCUMENT NUMBER: 124:139108
TITLE: The 18-kilodalton Chlamydia trachomatis histone H1-like protein (Hc1) contains a potential N-terminal dimerization site and a C-terminal nucleic acid-binding domain
AUTHOR(S): Pedersen, Lotte Bang; Birkelund, Svend; Holm, Arne; **Ostergaard, Soren**; Christiansen, Gunna
CORPORATE SOURCE: Department Medical Microbiology, University Aarhus, DK-8000, Den.
SOURCE: J. Bacteriol. (1996), 178(4), 994-1002
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Chlamydia trachomatis histone H1-like protein (Hc1) is a DNA-binding protein specific for the metabolically inactive chlamydial developmental form, the elementary body. Hc1 induces DNA condensation in Escherichia coli and is a strong inhibitor of transcription and translation. These effects may, in part, be due to Hc1-mediated alterations of DNA topol. To locate putative functional domains within Hc1, polypeptides Hc12-57 and Hc153-125, corresponding to the N- and C-terminal parts of Hc1, resp., were generated. By chem. crosslinking with ethylene glycol-bis(succinic

acid N-hydroxysuccinimide ester), purified recombinant Hc1 was found to form dimers. The dimerization site was located in the N-terminal part of Hc1 (Hc12-57). Moreover, CD measurements indicated an overall .alpha.-helical structure of this region. By using limited proteolysis, Southwestern blotting, and gel retardation assays, Hc153-225 was shown to contain a domain capable of binding both DNA and RNA. Under the same conditions, Hc12-57 had no nucleic acid-binding activity. Electron microscopy of Hc1-DNA and Hc153-125-DNA complexes revealed differences suggesting that the N-terminal part of Hc1 may affect the DNA-binding properties of Hc1.

L10 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:508605 HCAPLUS
DOCUMENT NUMBER: 123:105758
TITLE: Novel avidin and streptavidin binding sequences found in synthetic peptide libraries
AUTHOR(S): **Ostergaard, Soren**; Hansen, Per Hertz; Olsen, Marianne; Holm, Arne
CORPORATE SOURCE: Research Center for Medical Biotechnology, Chemistry Department Royal Veterinary and Agricultural University, Thorvaldsensvej 40, Copenhagen, DK-1871, Den.
SOURCE: FEBS Lett. (1995), 362(3), 306-8
CODEN: FEBLAL; ISSN: 0014-5793
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Synthetic resin-bound peptide libraries made of protein L-amino acids were synthesized. During screening of the libraries, peptides that bind to avidin were identified contg. a novel motif with 2 histidines sepd. by 1 residue. A sublibrary was synthesized and screened, and new crit. residues appeared surrounding the 2 histidines. Addnl. peptide libraries made of L-amino acids were screened with avidin and streptavidin and novel motifs found.

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L9 10 SEA FILE=HCAPLUS ABB=ON PLU=ON "JORGENSEN R"/AU OR "JORGENSEN R M"/AU OR "JORGENSEN RIKKE MALENE"/AU OR "JORGENSEN RIKKE MALENE"/IN
L10 19 SEA FILE=HCAPLUS ABB=ON PLU=ON "OSTERGAARD S"/AU OR ("OSTERGAARD SOREN"/AU OR "OSTERGAARD SOREN"/IN)
L12 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 NOT L10

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L12 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:776352 HCAPLUS
DOCUMENT NUMBER: 134:66270
TITLE: Creation of a selective antagonist and agonist of the rat VPAC1 receptor using a combinatorial approach with vasoactive intestinal peptide 6-23 as template
AUTHOR(S): Tams, Jeppe Wegener; **Jorgensen, Rikke Malene**; Holm, Arne; Fahrenkrug, Jan
CORPORATE SOURCE: Department of Clinical Biochemistry, Bispebjerg Hospital, Copenhagen, Den.
SOURCE: Mol. Pharmacol. (2000), 58(5), 1035-1041
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental

Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have used combinatorial chem. with amino acid mixts. (X) at positions 6 to 23 in vasoactive intestinal peptide (VIP) to optimize binding affinity and selectivity to the rat VPAC1 receptor. The most efficient amino acid replacement was a substitution of alanine at position 18 to diphenylalanine (Dip), increasing the displacement efficiency of 125I-VIP by 370-fold. The [Dip18]VIP(6-23) was subsequently used to find a second replacement, employing the same approach. Tyrosine at position 9 was selected and the resulting [Tyr9,Dip18]VIP(6-23) analog has a Ki value of 90 nM. This analog was unable to stimulate cAMP prodn. at 10-6 M but was able to inhibit VIP-induced cAMP stimulation (Kb = 79 nM). The Ki values of [Tyr9,Dip18]VIP(6-23) using the rat VPAC2 and PAC1 receptors were 3000 nM and >10,000 nM, resp. Thus, [Tyr9,Dip18]VIP(6-23) is a selective VPAC1 receptor antagonist. The C-terminally extended form, [Tyr9,Dip18]VIP(6-28), displays improved antagonistic properties having a Ki and Kb values of 18 nM and 16 nM, resp. On the contrary, the fully extended form, [Tyr9,Dip18]VIP(1-28), was a potent agonist with improved binding affinity (Ki = 0.11 nM) and ability to stimulate cAMP (EC50 = 0.23 nM) compared with VIP (Ki = 1.7 nM, EC50 = 1.12 nM). Furthermore, the specificity of this agonist to the VPAC1 receptor was high, the Ki values for the VPAC2 and PAC1 receptors were 53 nM and 3, 100 nM, resp. Seven other analogs with the [Tyr9,Dip18] replacement combined with previously published VIP modifications have been synthesized and described in this work.
REFERENCE COUNT: 27
REFERENCE(S):
(1) Arimura, A; Jpn J Physiol 1998, V48, P301 HCAPLUS
(3) Cheng, Y; Biochem Pharmacol 1973, V22, P3099 HCAPLUS
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(7) Gaddum, J; Pharmacol Rev 1957, V9, P211 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:352774 HCAPLUS
DOCUMENT NUMBER: 134:126665
TITLE: Assignment of the human mitochondrial translational release factor 1 (MTRF1) to chromosome 13q14.1.fwdarw.q14.3 and of the human mitochondrial ribosome recycling factor (MRRF) to chromosome 9q32.fwdarw.q34.1 with radiation hybrid mapping
AUTHOR(S): Hansen, L. L.; **Jorgensen, R.**; Justesen, J.
CORPORATE SOURCE: Institute of Human Genetics, Aarhus University, Aarhus, DK-8000, Den.
SOURCE: Cytogenet. Cell Genet. (2000), 88(1-2), 91-92
CODEN: CGCGBR; ISSN: 0301-0171
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ribosome recycling factor MRRF is a nuclear encoded mitochondrial protein, which is necessary for recycling of ribosomes after the termination of a peptide chain catalyzed by the mitochondrial translation release factor 1 (MTRF1). MRRF- and MTRF1-specific PCR primers and the Genebridge radiation hybrid panel were used to map the MRRF gene to human chromosome 9q32.fwdarw.q34.1 and the MTRF1 gene to chromosome 13q14.1.fwdarw.q14.3.
REFERENCE COUNT: 1
REFERENCE(S):
(1) Zhang, Y; Biochim biophys Acta 1998, V1443, P245 HCAPLUS

L12 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:423354 HCAPLUS
DOCUMENT NUMBER: 131:119904
TITLE: Methodology for hydrocarbon speciation for heavy duty diesel engines operating over the European ECE R49 cycle
AUTHOR(S): Reynolds, E. G.; Hall, D. E.; **Jorgensen, R.**; Kvinge, F.
CORPORATE SOURCE: BP Oil, USA
SOURCE: Soc. Automot. Eng., [Spec. Publ.] SP (1999), SP-1459(Topics in General Emissions), 95-99
CODEN: SAESA2; ISSN: 0099-5908
PUBLISHER: Society of Automotive Engineers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A methodol. has been developed to enable a single, gaseous sample to be collected from the dild. exhaust stream of heavy duty diesel engines operating over the European 13 mode ECE R49 emission cycle. The sample consists of timed contributions of dil. exhaust gas from each mode (weighted appropriately) to provide a gas sample that is representative of the complete cycle. The sample is collected in a Tedlar bag prior to GC anal. for individual hydrocarbon speciation. This methodol. has also been extended to allow for the collection of a representative carbonyl sample using 2,4-dinitrophenylhydrazine (2,4-DNPH) impregnated cartridges. Results obtained from these systems are reported and compared to results obtained from light duty (diesel and gasoline) investigations.
REFERENCE COUNT: 7
REFERENCE(S): (1) AQIRP (US Auto/Oil Quality Improvement Research Programme; SAE SP-1000 and SAE SP-920 1993
(2) Bennett, P; SAE961901
(3) European Commission; European Programme on Emissions Fuels and Engine Technology EPEFE 1996
(4) International Agency for Research on Cancer; IARC Group 1 1987
(5) International Agency for Research on Cancer; IARC Group 2A 1998
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:252182 HCAPLUS
DOCUMENT NUMBER: 116:252182
TITLE: Conditional male fertility in chalcone synthase-deficient petunia
AUTHOR(S): Taylor, L. P.; **Jorgensen, R.**
CORPORATE SOURCE: Dep. Hortic. Landscape Archit., Washington State Univ., Pullman, WA, 99164-6414, USA
SOURCE: J. Hered. (1992), 83(1), 11-17
CODEN: JOHEA8; ISSN: 0022-1503
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Transgenic petunia plants with suppressed chalcone synthase gene expression produce abnormal anthers devoid of flavonoid pigments. Although viable pollen is produced, pollen germination, and tube growth are severely reduced both in vivo and in vitro. This results in plants that are self-sterile. Pollen from the transgenic plants is partially rescued by inbred V26 stigmas, resulting in seed set that is approx. 30% of normal. Female fertility in the transgenic petunia is unaffected by the lack of flavonoids. The term conditional male fertility (CMF) is proposed to describe the state in which viable but flavonoid-deficient pollen does not function in self-crosses and is partially functional on wild-type stigmas. Although this condition has attributes of both male sterility and self-incompatibility, it is clearly different. This observation in petunia has similarities to the earlier report of Coe et

al. (1981) that most pollinations made with chalcone synthase (CHS)-deficient maize pollen were unsuccessful. The possibility that normal development of the male gametophyte requires flavonoid synthesis in many or all higher plants is discussed. The dominant CHS deficiency and male sterility in petunia, taken together with the recessive CHS deficiency and male sterility in maize, suggest that flavonoid synthesis in the sporophyte rather than the gametophyte is required for fertility.

L12 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1978:185977 HCAPLUS
DOCUMENT NUMBER: 88:185977
TITLE: Transposable neomycin phosphotransferases
AUTHOR(S): Davies, Julian; Berg, D.; **Jorgensen, R.**; Fiandt, M.; Huang, T. S. R.; Courvalin, P.; Schloff, J.
CORPORATE SOURCE: Dep. Biochem., Univ. Wisconsin, Madison, Wis., USA
SOURCE: Top. Infect. Dis. (1977), 2(R-Factors: Their Prop. Possible control), 101-14
CODEN: TIDID3
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Of the transposons which contain genes for resistance to aminoglycoside antibiotics, 3 encode aminoglycoside 3'-phosphotransferase: Tn6, Tn601, and Tn5. The Tn6 insertion in the .lambda. phage genome is unstable, whereas Tn5 and Tn601 are much more stable. Tn5 is transposed from .lambda. to the Escherichia coli chromosome, and from 1 chromosomal site to another, at high frequency. A phys. map for Tn5 insertions in the lacZ gene of E. coli is presented.

L12 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1978:166548 HCAPLUS
DOCUMENT NUMBER: 88:166548
TITLE: Genetic organization in the transposable tetracycline resistance determinant Tn10
AUTHOR(S): **Jorgensen, R.**; Berg, D.; Reznikoff, W.
CORPORATE SOURCE: Coll. Agric. Life Sci., Univ. Wisconsin, Madison, Wis., USA
SOURCE: Microbiology (Washington, D. C.) (1978) 181-3
CODEN: MICRDG; ISSN: 0098-1540
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Restriction endonuclease fragments of phage .lambda. bearing the 9400-base-pair tetracycline (I)-resistance transposon Tn10 were inserted into plasmid pVH51, and Escherichia coli recipients were transformed with the resulting plasmids. Plasmid DNA from 8 I-resistant clones was isolated and mapped with restriction endonucleases. All 8 plasmids had a common 2025-base-pair fragment which must represent the genes for I-resistance. The min. inhibitory concn. of I for the hosts varied, so sequences outside fragment 2025 must also play a role in regulating resistance.

L12 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1974:476611 HCAPLUS
DOCUMENT NUMBER: 81:76611
TITLE: Changes in milk, whey, and blue cheese as induced by benzoyl peroxide
AUTHOR(S): Washam, C. J.; Reinbold, G. W.; Vedamuthu, E. R.; **Jorgensen, R.**
CORPORATE SOURCE: Iowa State Univ., Ames, Iowa, USA
SOURCE: J. Milk Food Technol. (1974), 37(2), 244-9
CODEN: JMFTAT
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Heating of whey proteins (60.degree. for 2 hr) in the presence of benzoyl peroxide had a pronounced effect on the proteins, but polyacrylamide gel electrophoresis revealed changes in proteins not attributable to heat alone. Benzoyl peroxide-heat treated cheeses tended to expel moisture during leakage tests. During blue cheese manuf., benzoyl peroxide at 17.8 ppm whitened the cheese more than at 5.9 ppm, and this was true even when heat treatment was omitted. Use of benzoyl peroxide in the bleaching process did not decrease mold development in ripening loaves nor was acid prodn. by lactic cultures diminished. In addn., proteolysis of milk proteins by rennet was not reduced by benzoyl peroxide.

L12 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1967:405343 HCAPLUS
DOCUMENT NUMBER: 67:5343
TITLE: Nonmagnetic interconnect material for welded modules
AUTHOR(S): **Jorgensen, R. M.**
CORPORATE SOURCE: California Inst. of Technol., Pasadena, Calif., USA
SOURCE: NASA (Nat. Aeronaut. Space Admin.) Access. (1965), NASA-CR-64605, 90-3 Avail.: CFSTI, $3 cy
From: Sci. Tech. Aerospace Rept. 1965, 3(21), N65-32430
CODEN: NAACAF
DOCUMENT TYPE: Report
LANGUAGE: English
AB While many materials are nonmagnetic, very few approach Ni in terms of its utility as an interconnect material for welded cordwood. The unique characteristics of Ni that lend themselves to a welding interconnect are discussed and the classes of materials which may be investigated in order to find a nonmagnetic material to replace Ni are considered. An exptl. approach to detg. the feasibility of materials is based upon choosing the same conductor cross section that has been found to be optimum for Ni and comparting the results obtained to the weldability of Ni. The optimum Ni conductor cross section is 0.010 by 0.030 in.2 and this size is compatible with 0.017 to 0.040-in. diam. gold-plated Kovar; 0.016 to 0.030-in. diam. Dumet; 0.016 to 0.032-inch diam. Ni; 0.016 to 0.032-in. diam. O-free Cu; and 0.020 to 0.032-in. diam. ETP Cu wires when cross-wire welded. It is noted that Ni is close to being an ideal material in regard to ductility and freedom from weld-zone embrittlement. Therefore equaling the weldability of Ni may not be easy.

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L8 146 SEA FILE=HCAPLUS ABB=ON PLU=ON ("HOLM ARNE"/AU OR "HOLM ARNE"/IN)
L9 10 SEA FILE=HCAPLUS ABB=ON PLU=ON "JORGENSEN R"/AU OR "JORGENSEN R M"/AU OR "JORGENSEN RIKKE MALENE"/AU OR "JORGENSEN RIKKE MALENE"/IN
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L14 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:787484 HCAPLUS
DOCUMENT NUMBER: 130:181185
TITLE: Peptide-based OspC enzyme-linked immunosorbent assay for serodiagnosis of Lyme borreliosis
AUTHOR(S): Mathiesen, Marianne J.; Christiansen, Michael; Hansen, Klaus; **Holm, Arne**; Asbrink, Eva; **Theisen, Michael**
CORPORATE SOURCE: Department of Clinical Biochemistry, Statens Serum Institut, Copenhagen, DK-2300, Den.
SOURCE: J. Clin. Microbiol. (1998), 36(12), 3474-3479
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sera from 210 patients with Lyme borreliosis (LB) were studied by an ELISA based on a synthetic peptide (pepC10) comprising the C-terminal 10-amino-acid residues of OspC of Borrelia burgdorferi. The authors found that 36.3 and 45.0% of the serum samples from patients with erythema migrans (EM) and neuroborreliosis (NB), resp., displayed IgM anti-pepC10 reactivities, while these samples rarely (.ltoreq.8%) displayed IgG antibody reactivities. Sera from patients with acrodermatitis chronica atrophicans did not contain anti-pepC10 antibodies. The diagnostic performance of this newly developed peptide ELISA was compared with those of an ELISA based on the full-length recombinant OspC protein (rOspC) and a com. available ELISA based on the B. burgdorferi flagellum (Fla). The sensitivity of the IgM pepC10 ELISA was slightly lower than that of the rOspC ELISA for EM patients (36.3 vs. 43.8%), while there was no difference for NB patients (45.0 vs. 48.0%). However, the optical d. values obtained by the pepC10 ELISA were generally higher than those obtained by the rOspC ELISA, leading to a significantly better quant. discrimination between seropos. patients with NB and controls. The specificity of the pepC10 ELISA was similar to those of the rOspC ELISA and the Fla ELISA for relevant controls including patients with syphilis and mononucleosis. Although the overall diagnostic sensitivity of the Fla ELISA was superior, 8.8 and 12.0% of the EM and NB patients, resp., were antibody pos. only by the pepC10 ELISA. Thus, use of a diagnostic test for LB based on the detection of IgM antibodies to pepC10 and Fla has increased sensitivity for the diagnosis of early LB.
REFERENCE COUNT: 43
REFERENCE(S): (3) Altschul, S; J Mol Biol 1990, V215, P403 HCAPLUS
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(8) Dressler, F; J Infect Dis 1994, V169, P313 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d stat que l15
L7 63 SEA FILE=HCAPLUS ABB=ON PLU=ON ("HOLM A"/AU OR "HOLM A"/IN)
L8 146 SEA FILE=HCAPLUS ABB=ON PLU=ON ("HOLM ARNE"/AU OR "HOLM ARNE"/IN)
L9 10 SEA FILE=HCAPLUS ABB=ON PLU=ON "JORGENSEN R"/AU OR "JORGENSEN R M"/AU OR "JORGENSEN RIKKE MALENE"/AU OR "JORGENSEN RIKKE MALENE"/IN
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               MICHAEL"/AU OR "THEISEN MICHAEL"/IN OR "THEISEN MICHAEL J"/AU)
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L13            41 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 NOT (L10 OR L12)
L14             1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L13 AND (L7 OR L8)
L15            19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L13 AND (ANTIGEN? OR
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               OR PROTEIN)(W)SYSTEM?)) NOT L14


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L15  ANSWER 1 OF 19  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2000:829948  HCAPLUS
DOCUMENT NUMBER:          134:112771
TITLE:                    Conservation and heterogeneity of the glutamate-rich
                          protein (GLURP) among field isolates and laboratory
                          lines of Plasmodium falciparum
AUTHOR(S):                Stricker, K. D.; Vuust, J.; Jepsen, S.; Oeuvray, C.;
                          Theisen, M.
CORPORATE SOURCE:         Department of Clinical Biochemistry, Statens Serum
                          Institut, Copenhagen, DK-2300, Den.
SOURCE:                   Mol. Biochem. Parasitol. (2000), 111(1), 123-130
                          CODEN: MBIPDP; ISSN: 0166-6851
PUBLISHER:                Elsevier Science Ireland Ltd.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Genetic variation of the glutamate-rich protein (GLURP) of Plasmodium
     falciparum was analyzed in 29 field isolates and 15 lab. lines of diverse
     geog. origin, by DNA sequencing of the non-repetitive 5'-region (R0) of
     the glurp gene.  Polymorphism with respect to the length of the GLURP R2
     repeat region was also analyzed by a polymerase chain reaction method.  As
     ref., the nucleotide sequence of the highly polymorphic 3'-region of the
     circumsporozoite protein gene was detd. in the same isolates.  It was
     found that even in the presence of variations in the GLURP R2 repeat
     region, immunodominant parts of the GLURP R0 region are surprisingly well
     conserved and the conservation is most pronounced in isolates from
     locations with very high malaria transmission.  This might indicate that
     the R0 structure plays an important role in the parasite.
REFERENCE COUNT:          30
REFERENCE(S):             (4) Bouharoun-Tayoun, H; J Exp Med 1995, V182, P409
                              HCAPLUS
                          (5) Dodoo, D; J Infect Dis 2000, V181, P1202 HCAPLUS
                          (6) Doolan, D; Infect Immun 1992, V60, P675 HCAPLUS
                          (7) Dziegiel, M; Infect Immun 1993, V61, P103 HCAPLUS
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                          ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15  ANSWER 2 OF 19  HCAPLUS  COPYRIGHT 2001 ACS
ACCESSION NUMBER:         2000:526193  HCAPLUS
DOCUMENT NUMBER:          134:264768
TITLE:                    Identification of a major B-cell epitope of the
                          Plasmodium falciparum glutamate-rich protein (GLURP),
                          targeted by human antibodies mediating parasite
                          killing
AUTHOR(S):                Theisen, M.; Soe, S.; Jessing, S. G.;
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Okkels, L. M.; Danielsen, S.; Oeuvray, C.; Druilhe, P.; Jepsen, S.
CORPORATE SOURCE: Dep. Clinical Biochem., Statens Serum Inst., Copenhagen, Den.
SOURCE: Vaccine (2000), 19(2-3), 204-212
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **antigenicity** of the glutamate-rich protein (GLURP) of Plasmodium falciparum was comprehensively evaluated in epitope-mapping studies utilizing a phage display library, synthetic peptides and anti-GLURP IgG prepns. previously shown to promote strong antibody-dependent cellular inhibition (ADCI) effects. We identified six major B-cell epitopes within the nonrepetitive region R0, corresponding to amino acid residues 173 to 187 (P1), 193 to 207 (P3), 216 to 229 (P4), 264 to 288 (P11), 343 to 357 (P10), and 407 to 434 (S3). Of these, four (P1, P3, P4, and S3) were frequently recognized by high-titered IgG antibodies in plasma samples from immune Liberian adults (prevalence: 29.1-45.0%). The three epitopes P1, P3, and P4 contained a common motif (seven out of nine positions are identical) and may thus constitute a family of structurally related epitopes. This leaves two distinct epitopes, one (P3) representing this new epitope family and S3 as targets for biol. active antibodies. Human IgG antibodies from single plasma samples were affinity-purified against these peptides. P3-specific IgG prepns. were consistently more effective in ADCI than S3-specific IgG. Among the different GLURP epitopes, we therefore suggest that the P3 epitope is potentially the most important epitope in GLURP for the development of clin. immunity to malaria in man.
REFERENCE COUNT: 28
REFERENCE(S): (5) Bouharoun-Tayoun, H; J Exp Med 1995, V182, P409 HCAPLUS
(9) Druilhe, P; Immunol Lett 1994, V41, P115 HCAPLUS
(11) Dziegiel, M; Infect Immun 1993, V61, P103 HCAPLUS
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(15) Khusmith, S; Infect Immun 1983, V41, P219 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:358998 HCAPLUS
DOCUMENT NUMBER: 133:118838
TITLE: **Antigenic** equivalence of human T-cell responses to Mycobacterium tuberculosis-specific RD1-encoded protein **antigens** ESAT-6 and culture filtrate protein 10 and to mixtures of synthetic peptides
AUTHOR(S): Arend, Sandra M.; Geluk, Annemieke; Van Meijgaarden, Krista E.; Van Dissel, Jaap T.; **Theisen, Michael**; Andersen, Peter; Ottenhoff, Tom H. M.
CORPORATE SOURCE: Department of Infectious Diseases, Leiden University Medical Center, Leiden, 2300, Neth.
SOURCE: Infect. Immun. (2000), 68(6), 3314-3321
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The early secreted **antigenic** target 6-kDa protein (ESAT-6) and culture filtrate protein 10 (CFP-10) are promising **antigens** for reliable immunodiagnosis of tuberculosis. Both **antigens** are encoded by RD1, a genomic region present in all strains of Mycobacterium tuberculosis and M. bovis but lacking in all M. bovis bacillus Calmette-Guerin vaccine strains. Prodn. and purifn. of recombinant

antigens are laborious and costly, precluding rapid and large-scale testing. Aiming to develop alternative diagnostic reagents, we have investigated whether recombinant ESAT-6 (rESAT-6) and recombinant CFP-10 (rCFP-10) can be replaced with corresponding mixts. of overlapping peptides spanning the complete amino acid sequence of each **antigen**. Proliferation of M. tuberculosis-specific human T-cell lines in response to rESAT-6 and rCFP-10 and that in response to the corresponding peptide mixts. were almost completely correlated ($r = 0.96$, $P < 0.0001$ for ESAT-6; $r = 0.98$, $P < 0.0001$ for CFP-10). More importantly, the same was found when gamma interferon prodn. by peripheral blood mononuclear cells in response to these stimuli was analyzed ($r = 0.89$, $P < 0.0001$ for ESAT-6; $r = 0.89$, $P < 0.0001$ for CFP-10). Whole protein **antigens** and the peptide mixts. resulted in identical sensitivity and specificity for detection of infection with M. tuberculosis. The peptides in each mixt. contributing to the overall response varied between individuals with different HLA-DR types. Interestingly, responses to CFP-10 were significantly higher in the presence of HLA-DR15, which is the major subtype of DR2. These results show that mixts. of synthetic overlapping peptides have potency equiv. to that of whole ESAT-6 and CFP-10 for sensitive and specific detection of infection with M. tuberculosis, and peptides have the advantage of faster prodn. at lower cost.

REFERENCE COUNT: 30

REFERENCE(S):
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(9) Brosch, R; Infect Immun 1998, V66, P2221 HCAPLUS
(10) Cole, S; Nature 1998, V393, P537 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:287414 HCAPLUS

DOCUMENT NUMBER: 133:295081

TITLE: Naturally acquired antibodies to the glutamate-rich protein are associated with protection against Plasmodium falciparum malaria

AUTHOR(S): Dodoo, Daniel; **Theisen, Michael**; Kurtzhals, Jorgen A. L.; Akanmori, Bartholomew D.; Koram, Kwadwo A.; Jepsen, Soren; Nkrumah, Francis K.; Theander, Thor G.; Hviid, Lars

CORPORATE SOURCE: Immunology and Epidemiology Units, University of Ghana, Legon, Ghana

SOURCE: J. Infect. Dis. (2000), 181(3), 1202-1205
CODEN: JIDIAQ; ISSN: 0022-1899

PUBLISHER: University of Chicago Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The development of effective malaria vaccines depends on the identification of targets of well-defined protective immune responses. Data and samples from a longitudinal study of a cohort of children from coastal Ghana were used to investigate the role of antibody responses to 3 regions of the Plasmodium falciparum glutamate-rich protein (GLURP). These data show that levels of the GLURP-specific IgG that occurs in the nonrepeat region of the **antigen** are significantly correlated with clin. protection from P. falciparum malaria, after correction for the confounding effect of age. Furthermore, levels of cytophilic antibodies were found to be of particular importance for protection, lending support to the hypothesis that antibody-dependent cellular inhibition is the important element in GLURP-specific protective immunity.

REFERENCE COUNT: 14

REFERENCE(S):
(3) Bouharoun-Tayoun, H; Infect Immun 1992, V60, P1473 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:282549 HCAPLUS
DOCUMENT NUMBER: 133:41887
TITLE: Cytophilic immunoglobulin responses to Plasmodium falciparum glutamate-rich protein are correlated with protection against clinical malaria in Dielmo, Senegal
AUTHOR(S): Qeuvray, Claude; **Theisen, Michael**; Rogier, Christophe; Trape, Jean-Francois; Jepsen, Soren; Druilhe, Pierre
CORPORATE SOURCE: Laboratoire de Parasitologie BioMedicale, Institut Pasteur, Paris, 75015, Fr.
SOURCE: Infect. Immun. (2000), 68(5), 2617-2620
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The goal of this study was to analyze antibody responses to Plasmodium falciparum glutamate-rich protein (GLURP) using clin. data and plasma samples obtained from villagers of Dielmo, Senegal. This mol. was chosen because it is targeted by human antibodies which induce parasite growth inhibition in antibody-dependent cellular inhibition (ADCI) assays. The results showed a strong correlation between protection against malaria attacks and levels of IgG2 and IgG3 against GLURP94-489 (R0) and IgG3 against GLURP705-1178 (R2) when cor. for the confounding effect of age-related exposure to malaria. Thus, GLURP may play a role in the induction of protective immunity against P. falciparum malaria.
REFERENCE COUNT: 23
REFERENCE(S): (4) Bouharoun-Tayoun, H; Infect Immun 1992, V60, P1473 HCAPLUS
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(16) Sarthou, J; Infect Immun 1997, V65, P3271 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:155853 HCAPLUS
DOCUMENT NUMBER: 132:304796
TITLE: Triple helix **assembly** and processing of human collagen produced in transgenic tobacco plants
AUTHOR(S): Ruggiero, F.; Exposito, J.-Y.; Bournat, P.; Gruber, V.; Perret, S.; Comte, J.; Olagnier, B.; Garrone, R.; **Theisen, M.**
CORPORATE SOURCE: Institut de Biologie et Chimie des Proteines, CNRS UPR 412, Universite Lyon I, Lyon, F-69367, Fr.
SOURCE: FEBS Lett. (2000), 469(1), 132-136
CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The use of tobacco plants as a novel expression system for the prodn. of human homotrimeric collagen I is presented in this report. Constructs were engineered from cDNA encoding the human pro.alpha.1(I) chain to generate transgenic tobacco plants expressing collagen I. The recombinant pro.alpha.1(I) chains were expressed as disulfide-bonded trimers and were shown to fold into a stable homotrimeric triple helix. Moreover, the recombinant procollagen was subsequently processed to collagen as it

occurs in animals. Large amts. of recombinant collagen were purified from field grown plant material. The data suggest that plants are a valuable alternative for the recombinant prodn. of collagen for various medical and scientific purposes.

REFERENCE COUNT: 27

REFERENCE(S):
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(4) Denecke, J; Plant Cell 1995, V7, P391 HCAPLUS
(6) Elefteriou, F; J Biol Chem 1997, V272, P22866 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:765518 HCAPLUS

DOCUMENT NUMBER: 132:75375

TITLE: Crystal structure of SQD1, an enzyme involved in the biosynthesis of the plant sulfolipid headgroup donor UDP-sulfoquinovose

AUTHOR(S): Mulichak, Anne M.; **Theisen, Michael J.**; Essigmann, Bernd; Benning, Christoph; Garavito, R. Michael

CORPORATE SOURCE: Department of Biochemistry, Michigan State University, East Lansing, MI, 48824-1319, USA

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1999), 96(23), 13097-13102
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The SQD1 enzyme is believed to be involved in the biosynthesis of the sulfoquinovosyl headgroup of plant sulfolipids, catalyzing the transfer of SO3- to UDP-glucose. We have detd. the structure of the complex of SQD1 from Arabidopsis thaliana with NAD+ and the putative substrate UDP-glucose at 1.6-.ANG. resoln. Both bound **ligands** are completely buried within the binding cleft, along with an internal solvent cavity which is the likely binding site for the, as yet, unidentified sulfur-donor substrate. SQD1 is a member of the short-chain dehydrogenase/reductase (SDR) family of enzymes, and its structure shows a conservation of the SDR catalytic residues. Among several highly conserved catalytic residues, Thr-145 forms unusually short hydrogen bonds with both susceptible hydroxyls of UDP-glucose. A His side chain may also be catalytically important in the sulfonation.

REFERENCE COUNT: 48

REFERENCE(S):
(1) Baker, M; FEBS Lett 1992, V301, P89 HCAPLUS
(2) Benning, C; Annu Rev Plant Physiol Plant Mol Biol 1998, V49, P53 HCAPLUS
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(4) Benning, C; J Bacteriol 1992, V174, P6479 HCAPLUS
(5) Benning, C; Proc Natl Acad Sci USA 1993, V90, P1561 HCAPLUS

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L15 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1999:750692 HCAPLUS

DOCUMENT NUMBER: 132:235685

TITLE: IgG reactivities against recombinant rhoptry-associated protein-1 (rRAP-1) are associated with mixed Plasmodium infections and protection against disease in Tanzanian children

AUTHOR(S): Alifrangis, M.; Lemnge, M. M.; Moon, R.; **Theisen, M.**; Bygbjerg, I.; Ridley, R. G.; Jakobsen, P. H.

CORPORATE SOURCE: Centre for Medical Parasitology, Institute of Medical Microbiology and Immunology, Panum Institute, University of Copenhagen, Copenhagen, 2200, Den.
SOURCE: Parasitology (1999), 119(4), 337-342
CODEN: PARAAE; ISSN: 0031-1820
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A cross-sectional sero-epidemiol. study was performed in Magoda, Tanzania, an area where malaria is holoendemic. Blood samples were collected from children (1-4 yr) and tested for IgG antibody reactivity against 2 recombinant protein fragments of Plasmodium falciparum Rhoptry-Assocd. Protein-1 (rRAP-1). The data were related to the prevalence of malarial disease and single P. falciparum or mixed Plasmodium infections. Fever (.gtoreq.37.5.degree.) in combination with parasite densities >5000/.mu.l were used to distinguish between children with asymptomatic malaria infections and those with acute clin. disease. Furthermore, C-reactive protein (CRP) was applied as a surrogate marker of malaria morbidity. The prevalence of Plasmodium infections was 96.0%. Eleven children were defined as clin. malaria cases, all with single P. falciparum infections. The d. of P. falciparum was significantly lower in children with mixed Plasmodium infections compared to those with single P. falciparum infections. Children with asymptomatic P. falciparum infections had higher IgG reactivities to rRAP-1, compared to IgG reactivities of children with malarial disease. Children with mixed Plasmodium infections generally showed elevated IgG reactivity to rRAP-1, when compared to children with single P. falciparum infections. The possible relationship between mixed species infections, clin. outcome of the disease and antibody responses to RAP-1 is discussed.

REFERENCE COUNT: 18
REFERENCE(S):
(3) Beck, H; Journal of Infectious Diseases 1997, V175, P921 HCAPLUS
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(9) Jakobsen, P; Immunology Letters 1997, V59, P35 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:363176 HCAPLUS
DOCUMENT NUMBER: 129:121333
TITLE: Identification and characterization of a 29-kilodalton protein from Mycobacterium tuberculosis culture filtrate recognized by mouse memory effector cells
AUTHOR(S): Rosenkrands, Ida; Rasmussen, Peter Birk; Carnio, Markus; Jacobsen, Susanne; **Theisen, Michael**; Andersen, Peter
CORPORATE SOURCE: Department of TB Immunology, Statens Serum Institut, Copenhagen S, DK-2300, Den.
SOURCE: Infect. Immun. (1998), 66(6), 2728-2735
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Culture filtrate proteins from Mycobacterium tuberculosis induce protective immunity in various animal models of tuberculosis. Two mol. mass regions (6 to 10 kDa and 24 to 36 kDa) of short-term culture filtrate are preferentially recognized by Th1 cells in animal models as well as by patients with minimal disease. In the present study, the 24- to 36-kDa

region has been studied, and the T-cell reactivity has been mapped in detail. Monoclonal antibodies were generated, and one monoclonal antibody, HYB 71-2, with reactivity against a 29-kDa **antigen** located in the highly reactive region below the **antigen** 85 complex was selected. The 29-kDa **antigen** (CFP29) was purified from M. tuberculosis short-term culture filtrate by thiophilic adsorption chromatog., anion-exchange chromatog., and gel filtration. In its native form, CFP29 forms a polymer with a high mol. mass. CFP29 was mapped in two-dimensional electrophoresis gels as three distinct spots just below the **antigen** 85 complex component MPT59. CFP29 is present in both culture filtrate and the membrane fraction from M. tuberculosis, suggesting that this **antigen** is released from the envelope to culture filtrate during growth. Detn. of the N-terminal amino acid sequence allowed cloning and sequencing of the cfp29 gene. The nucleotide sequence showed 62% identity to the bacteriocin Linocin from Brevibacterium linens. Purified recombinant histidine-tagged CFP29 and native CFP29 had similar T-cell stimulatory properties, and they both elicited the release of high levels of gamma interferon from mouse memory effector cells isolated during the recall of protective immunity to tuberculosis. Interspecies anal. by immunoblotting and PCR demonstrated that CFP29 is widely distributed in mycobacterial species.

L15 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:117548 HCAPLUS
DOCUMENT NUMBER: 128:216349
TITLE: Inflammatory reactions in placental blood of Plasmodium falciparum-infected women and high concentrations of soluble E-selectin and a circulating P. falciparum protein in the cord sera
AUTHOR(S): Jakobsen, P. H.; Rasheed, F. N.; Bulmer, J. N.; **Theisen, M.**; Ridley, R. G.; Greenwood, B. M.
CORPORATE SOURCE: Departments of Clinical Microbiology, Copenhagen University Hospital, Den.
SOURCE: Immunology (1998), 93(2), 264-269
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To better understand reasons for increased susceptibility to malaria in pregnancy and the interrelationships between maternal malaria, local immune reactions and the development of the fetus, concns. of sol. interleukin-10 (IL-10), cytokine receptors, adhesion mols., a Plasmodium falciparum protein, glutamate-rich protein (GLURP) and antibodies to P. falciparum rhoptry-assocd. protein-1 were measured among 105 Gambian women and their neonates. Peripheral blood concns. of IL-10, sol. cytokine receptors and sol. adhesion mols. were found to be different from those concns. measured in the placenta. Markers of inflammatory reactions: IL-10, sIL-2R, sIL-4R, and sol. tumor necrosis factor receptor I (sTNF-RI) were found in high concns. in the placenta, indicating that inflammatory reactions take place in the placenta which has been regarded as an immunoprivileged site. Concns. of sol. vascular cell adhesion mol.-1 (sVCAM-1) and sol. intracellular adhesion mol.-1 (sICAM-1), potential adhesion receptors for malaria parasites, were assocd. with an active P. falciparum infection in the placenta although the assocns. did not reach significance. P. falciparum exoantigen, GLURP, was detected in cord blood indicating transplacental passage of malarial **antigens**. Concns. of E-selectin were higher in cord blood samples compared with peripheral blood samples. This appeared to be assocd. with development of cord endothelial cells and not with P. falciparum infection.

L15 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:7799 HCAPLUS
DOCUMENT NUMBER: 128:113917

TITLE: The glutamate-rich protein (GLURP) of Plasmodium falciparum is a target for antibody-dependent monocyte-mediated inhibition of parasite growth in vitro
AUTHOR(S): **Theisen, Michael**; Soe, Soe; Oeuvray, Claude; Thomas, Alan W.; Vuust, Jens; Danielsen, Steffen; Jepsen, Soren; Druilhe, Pierre
CORPORATE SOURCE: Department of Clinical Biochemistry, Statens Seruminstitut, Copenhagen, DK-2300, Den.
SOURCE: Infect. Immun. (1998), 66(1), 11-17
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Monocyte-dependent as well as direct inhibitory effects of antimalarial antibodies point toward **antigens** accessible at the time of merozoite release as targets for biol. active antibodies capable of mediating protection against Plasmodium falciparum. The glutamate-rich protein (GLURP), being an **antigen** assocd. with mature schizont-infected erythrocytes, was therefore the object of the present investigation, in which the authors analyzed whether anti-GLURP antibodies can either interfere directly with merozoite invasion or act indirectly by promoting a monocyte-dependent growth inhibition, antibody-dependent cellular inhibition. GLURP-specific human IgG antibodies, from pooled IgG of healthy Liberian adults who were clin. immune to malaria, were purified by affinity chromatog. on columns contg. R0 (N-terminal non-repetitive region of GLURP) or R2 (C-terminal repetitive region of GLURP) recombinant protein or synthetic peptides as **ligands**. Anal. of the pattern of reactivity of highly purified anti-GLURP antibodies led to the definition of at least four B-cell epitopes. One epitope was specific for R0, two were specific for R2, and the fourth displayed cross-reactivity between R0 and R2. None of the purified IgG antibodies had direct invasion-inhibitory effects, even at high concns. In contrast, when allowed to cooperate with monocytes, all anti-GLURP IgG prepns. mediated a strong monocyte-dependent parasite growth inhibition in a dose-dependent manner.

L15 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:87580 HCAPLUS
DOCUMENT NUMBER: 126:143233
TITLE: Analysis of the human antibody response to outer surface protein C (OspC) of Borrelia burgdorferi sensu stricto, B. garinii, and B. afzelii
AUTHOR(S): Mathiesen, Marianne Jartved; Hansen, Klaus; Axelsen, Nils; Halkier-Soerensen, Lars; **Theisen, Michael**
CORPORATE SOURCE: Borrelia Laboratory, Department of Clinical Biochemistry, Copenhagen, DK-2300, Den.
SOURCE: Med. Microbiol. Immunol. (1996), 185(3), 121-129
CODEN: MMIYAO; ISSN: 0300-8584
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of this study was to det. by Western blotting (WB) the prevalence of anti-outer surface protein C (OspC) IgM and IgG antibodies in patients with Lyme borreliosis according to each of the three genospecies of Borrelia burgdorferi sensu lato. Strains of B. burgdorferi sensu stricto (MUL), B. garinii (DK 6), and B. afzelii (DK 26) served as **antigen**, all of which expressed abundant OspC. The authors examd. sera from 117 patients with untreated early and late Lyme borreliosis, as well as from 100 blood donors and 29 patients with syphilis. WB results were compared with the B. burgdorferi flagellum ELISA (ELISA) data. OspC from B. burgdorferi sensu stricto showed the lowest diagnostic sensitivity. OspC

from B. garinii and B. afzelii performed almost identically in erythema migrans, with an IgM pos. rate of 36 vs. 34%, whereas OspC from B. garinii performed best in neuroborreliosis (60 vs. 44%). The anti-OspC IgG response was less prominent than the IgM response and was infrequent in the late stages of the disease (0-20%). The benefit of combining the evaluation of anti-OspC responses with all three species was limited. The overall diagnostic sensitivity of WB anti-B. garinii OspC evaluation was, in the early stages of the disease, comparable to the results obtained using the flagellum ELISA. In erythema migrans and neuroborreliosis, the addn. of anti-OspC IgM to the flagellum ELISA increased the sensitivity by 15% and 10%, resp. It can, therefore, be concluded that OspC from B. garinii is a suitable OspC test **antigen**, and that supplementary use of OspC from other species adds little to the overall diagnostic sensitivity. An ELISA based on B. garinii OspC and native flagella seems currently the most promising concept for a future antibody test in early Lyme borreliosis.

L15 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:583277 HCAPLUS
DOCUMENT NUMBER: 123:138478
TITLE: Taxonomic classification of 29 Borrelia burgdorferi strains isolated from patients with Lyme borreliosis: A comparison of five different phenotypic and genotypic typing schemes
AUTHOR(S): Lebech, Anne-Mette; Hansen, Klaus; Wilske, Bettina; **Theisen, Michael**
CORPORATE SOURCE: Department Infection-Immunology, Statens Seruminstitut, Copenhagen, DK-2300, Den.
SOURCE: Med. Microbiol. Immunol. (1994), 183(6), 325-41
CODEN: MMIYAO; ISSN: 0300-8584
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Twenty-nine European and North American Borrelia burgdorferi strains isolated from patients with Lyme borreliosis, were investigated by restriction fragment length polymorphism (RFLP) of two phylogenetically highly conserved chromosomal genes encoding flagellin (fla) and the p60 common **antigen** (CA), as well as of the plasmid-borne outer surface protein A (ospA) gene. RFLP of the ospA, fla and CA genes revealed five, two and four distinct subspecies-specific patterns, resp. RFLP classification of the B. burgdorferi strains was compared with four different classification schemes proposed by others: (i) mol. mass profile of OspA and OspB (Adam et al. [1]); (ii) OspA serotyping (Wilske et al. [34]); (iii) genomic fingerprinting on the central region of the B. burgdorferi fla gene (Picken [24]) and (iv) 16S rRNA signature nucleotide anal. (Marconi and Garon [19]). Results obtained with the different methods correlated highly. All strains classified as B. burgdorferi sensu stricto and B. afzelii could be unequivocally identified as one distinct group by all five typing methods. B. garinii isolates, however, were more heterogeneous and according to RFLP of the CA and ospA gene fell into either two or three subgroups. The agreement of the different approaches supports the recent concept that B. burgdorferi sensu lato strains should be delineated to three genomic groups and that B. burgdorferi sensu lato is clonal. All 12 US strains were B. burgdorferi sensu stricto, whereas the 17 European isolates belonged to any of three genospecies. Among European B. burgdorferi isolates there was an assocn. between B. burgdorferi genospecies and the clin. manifestation of Lyme borreliosis. B. afzelii strains were found to predominate in 11 skin isolates (75%), whereas all 6 cerebrospinal fluid isolates from patients with neuroborreliosis were B. garinii. These findings support the concept of a strain-dependent organotropism of B. burgdorferi.

L15 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:431330 HCAPLUS

DOCUMENT NUMBER: 122:211558
TITLE: **Antigenicity** and immunogenicity of recombinant glutamate-rich protein of Plasmodium falciparum expressed in Escherichia coli
AUTHOR(S): **Theisen, Michael**; Vuust, Jens; Gottschau, Adam; Jepsen, Soeren; Hoegh, Birthe
CORPORATE SOURCE: Department Infection-Immunology, Statens Seruminstitut, Copenhagen, DK-2300, Den.
SOURCE: Clin. Diagn. Lab: Immunol. (1995), 2(1), 30-4
CODEN: CDIMEN; ISSN: 1071-412X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A recombinant Plasmodium falciparum glutamate-rich protein (GLURP) was produced in Escherichia coli as a nearly full-length protein. To map immunodominant regions on GLURP, the non-repetitive N-terminal region (R0) as well as the central repeat region (R1) and the C-terminal repeat region (R2) were also produced as sep. products. All four purified gene products reacted specifically with serum samples from adults living in an area of Liberia where malaria is holoendemic. It appears that the human immune response against GLURP is primarily directed against the R2 region because 94% of the serum samples reacted with this region in an immunoassay. Antibody reactivity against the R0 region was also obsd. in 75% of the serum samples, while the R1 region showed only weak antibody-binding activity. When the nearly full-length GLURP mol. was adsorbed to Al(OH)3 it was immunogenic in mice. In these expts., the antibody response was almost exclusively directed against the R2 region. When anti-GLURP sera were obtained from rabbits immunized with the three regions, R0, R1, and R2, resp., they recognized in immunopptn. expts. authentic GLURP from P. falciparum grown in vitro. These results demonstrate that GLURP produced in E. coli can induce a humoral immune response against GLURP derived from blood-stage parasites.

L15 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:262492 HCAPLUS
DOCUMENT NUMBER: 120:262492
TITLE: Polymorphism in ospC gene of Borrelia burgdorferi and immunoreactivity of OspC protein: implications for taxonomy and for use of OspC protein as a diagnostic **antigen**
AUTHOR(S): **Theisen, Michael**; Frederiksen, Birgitte; Lebech, Anne Mette; Vuust, Jens; Hansen, Klaus
CORPORATE SOURCE: Dep. Infect. Immunol., Statens Seruminst., Copenhagen, DK-2300, Den.
SOURCE: J. Clin. Microbiol. (1993), 31(10), 2570-6
CODEN: JCMIDW; ISSN: 0095-1137
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The nucleotide sequences of the ospC gene from five Danish human Borrelia burgdorferi isolates representing all three B. burgdorferi genospecies (B. burgdorferi sensu stricto, Borrelia garinii sp. nov., and group VS461) and from the American type strain B31 were detd. and compared with the published ospC sequence from the German B. burgdorferi isolate PKo (R. Fuchs, S. Jauris, F. Lottspeich, V. Preac-Mursic, B. Wilske, and E. Soutschek, Mol. Microbiol. 6:503-509, 1992). The ospC gene was present in all isolates, regardless of the presence or absence of its product, OspC. The deduced amino acid sequences of OspC from the seven isolates were aligned and revealed pairwise sequence identities ranging from 60.5 to 100%. Differences were scattered throughout the amino acid sequences. A phylogenetic tree was constructed and revealed three distinct phenotypic groups OspCI to OspCIII corresponding to the three delineated genospecies. Immunoblot anal. revealed that the seven OspC proteins tested have both common and specific epitopes. There is significant epitope diversity, since even polyclonal antisera showed serotype-restricted specificity.

Therefore, a serodiagnostic assay for Lyme borreliosis utilizing OspC as a test **antigen** should include all three OspC phenotypes in order to obtain a species-wide sensitivity.

L15 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:161622 HCAPLUS
DOCUMENT NUMBER: 120:161622
TITLE: **Antigenic** proteins of Haemophilus somnus for use in vaccines and cloning and expression of genes encoding them
INVENTOR(S): Potter, Andrew A.; Pontarollo, Reno A.; Pfeiffer, Cheryl G.; **Theisen, Michael**; Harland, Richard J.; Rioux, Clement
PATENT ASSIGNEE(S): University of Saskatchewan, Can.
SOURCE: PCT Int. Appl., 120 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9321323	A1	19931028	WO 1993-CA135	19930405
W: AU, CA, HU, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9338838	A1	19931118	AU 1993-38838	19930405
EP 635055	A1	19950125	EP 1993-907710	19930405
EP 635055	B1	19981223		
R: DE, FR, GB				
US 6100066	A	20000808	US 1996-619812	19960315

PRIORITY APPLN. INFO.:
US 1992-865050 A 19920409
US 1992-893424 A 19920604
US 1992-893426 A 19920604
US 1993-38287 A 19930329
US 1993-38288 A 19930329
US 1993-38719 A 19930329
WO 1993-CA135 A 19930405

AB **Antigenic** proteins of Haemophilus somnus including the hemin-binding protein, the hemolysin, and the LppB and LppC proteins are obtained. The proteins are used in vaccines and may be manufd. by heterologous expression of the cloned genes. The genes for the hemin-binding protein (hmb) and the hemolysin (hly) were cloned from a Sau3A partial digest library in pHC79 by screening for activity and the genes subcloned by std. methods. Similarly, several other genes were cloned by screening for activity, including LppA; this gene was cloned from a Sau 3A partial library in the expression vector pGH433 by screening with hyperimmune serum. The LppB gene was cloned by its conferring of Congo Red binding activity. The LppA and LppB proteins manufd. using these clones were extd. from inclusion bodies and incorporated into vaccines with Emulsigen Plus to give 2 mL prepns. contg. 100 .mu.g **antigen** and 33 vol.% adjuvant. Calves were innoculated twice at three week intervals with 2 mL of vaccine (LppA, or LppB, or LppA+LppB, or placebo) and the titers of antibodies showed that both proteins were **antigenic** and did not interfere with one another. The vaccinated animals showed less severe symptoms upon challenge with 108 cfu of H. somnus.

L15 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:464572 HCAPLUS
DOCUMENT NUMBER: 119:64572
TITLE: Molecular cloning, nucleotide sequence, and characterization of lppB, encoding an

antigenic 40-kilodalton lipoprotein of Haemophilus somnus

AUTHOR(S): **Theisen, Michael**; Rioux, Clement R.; Potter, Andrew A.

CORPORATE SOURCE: Vet. Infect. Dis. Organ., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.

SOURCE: Infect. Immun. (1993), 61(5), 1793-8
CODEN: INFIBR; ISSN: 0019-9567

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Hemopholus somnus is a facultative intracellular pathogen which causes a wide range of diseases in cattle. To identify putative virulence determinants, a genomic library of H. somnus in Escherichia coli was screened for Congo red binding, a property assocd. with virulence in pathogenic bacteria, and subsequently with bovine hyperimmune sera raised against H. somnus HS25. A Congo red-binding clone carrying a 1.8-kb DNA insert was found to encode a strongly seroreactive LppB protein with an apparent mol. wt. of 40,000. The nucleotide sequence of the entire DNA insert was detd. Two open reading frames coding for polypeptides with calcd. mol. wts. of 21,893 and 30,721 were identified. The larger open reading frame encoded LppB, while the smaller reading frame encoded a nonseroreactive protein with a relative mol. mass of approx. 18 kDa. The 16 amino-terminal amino acids of the deduced LppB polypeptide showed strong sequence homol. to the signal peptide of secreted bacterial proteins, and the sequence Leu-Ala-Ala-Cys at the putative cleavage site corresponds to the consensus cleavage sequence of bacterial lipoproteins. Synthesis of the mature LppB lipoprotein in H. somnus was inhibited by globomycin, a specific inhibitor of signal peptidase II. LppB was localized to the outer membrane of H. somnus.

L15 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1993:189453 HCAPLUS

DOCUMENT NUMBER: 118:189453

TITLE: Molecular cloning, nucleotide sequence, and characterization of a 40,000-molecular-weight lipoprotein of Haemophilus somnus

AUTHOR(S): **Theisen, Michael**; Rioux, Clement R.; Potter, Andrew A.

CORPORATE SOURCE: Vet. Infect. Dis. Organ., Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.

SOURCE: Infect. Immun. (1992), 60(3), 826-31
CODEN: INFIBR; ISSN: 0019-9567

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A gene of H. somnus encoding the major 40,000-mol.-wt. **antigen** (LppA) was cloned on a 2-kb SauAi fragment. The nucleotide sequence of the entire DNA insert was detd. One open reading frame, encoding a 247-residue polypeptide with a calcd. mol. wt. of 27,072, was identified. This reading frame was confirmed by sequencing the fusion joint of two independent lppA::TnphoA gene fusions. The 21 N-terminal amino acids of the deduced polypeptide showed strong sequence homol. to the signal peptide of secreted proteins, and the sequence Leu-Leu-Ala-Ala-Cys at the putative cleavage site is identical to the consensus cleavage sequence of lipoproteins from gram-neg. bacteria. The presence of the lipid moiety on the protein was shown by incorporation of radioactive palmitic acid into the natural H. somnus protein. Palmitic acid could also be incorporated into the recombinant protein in Escherichia coli. Synthesis of the mature LppA lipoprotein was inhibited by globomycin, showing that cleavage of the signal peptide is mediated by signal peptidase II in both organisms. By using site-directed mutagenesis, the cysteine residue at the cleavage site was changed to glycine. Radiolabeled palmitate was not incorporated into the mutated protein, showing that lipid modification occurs at the Cys-22 residue.

L15 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:53322 HCAPLUS
DOCUMENT NUMBER: 118:53322
TITLE: Cloning, sequencing, expression, and functional studies of a 15,000-molecular-weight Haemophilus somnus **antigen** similar to Escherichia coli ribosomal protein S9
AUTHOR(S): **Theisen, Michael**; Potter, Andrew A.
CORPORATE SOURCE: Univ. Saskatchewan, Saskatoon, SK, S7N 0W0, Can.
SOURCE: J. Bacteriol. (1992), 174(1), 17-23
CODEN: JOBAAY; ISSN: 0021-9193
DOCUMENT TYPE: Journal
LANGUAGE: English
AB H. somnus is a gram-neg. bacterium capable of causing a no. of disease syndromes in cattle. This article describes the cloning and characterization of a gene coding for a 15,000-mol.-wt. (15K) polypeptide which reacts strongly with antiserum against H. somnus. Anal. of plasmid-encoded polypeptides by polyacrylamide gel electrophoresis showed that the corresponding gene is the second in a transcriptional unit. The first gene codes for a protein with a mol. wt. of approx. 17,000. Using antiserum against the two recombinant proteins, the authors could show that the natural proteins are predominantly present in purified ribosomes from H. somnus. The nucleotide sequence of both genes and flanking regions has been detd., and the deduced amino acid sequence of the two polypeptides was used to search for sequence homol. in the GenBank data base. The 15K polypeptide showed 89% similarity to the E. coli ribosomal protein S9, and the 17K polypeptide showed 94% similarity to the E. coli ribosomal protein L13. In E. coli, the corresponding genes constitute a bicistronic operon, with the same gene order as that found in H. somnus. A plasmid expressing the 15K protein was found to complement an E. coli rpsI mutation. When a frameshift mutation was introduced into the 15K protein gene, the resulting plasmid failed to complement this rpsI mutation, demonstrating functional homol. between the 15K protein and S9 from E. coli. Downstream from the 15K protein gene is located another open reading frame, which could code for a polypeptide with a predicted mol. wt. of 24,427. A protein with a similar mol. wt. was detected in minicells contg. the recombinant clone. This polypeptide is 69% similar to the stringent starvation protein (Ssp) of E. coli.

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L7 63 SEA FILE=HCAPLUS ABB=ON PLU=ON ("HOLM A"/AU OR "HOLM A"/IN)
L8 146 SEA FILE=HCAPLUS ABB=ON PLU=ON ("HOLM ARNE"/AU OR "HOLM ARNE"/IN)
L9 10 SEA FILE=HCAPLUS ABB=ON PLU=ON "JORGENSEN R"/AU OR "JORGENSEN R M"/AU OR "JORGENSEN RIKKE MALENE"/AU OR "JORGENSEN RIKKE MALENE"/IN
L10 19 SEA FILE=HCAPLUS ABB=ON PLU=ON "OSTERGAARD S"/AU OR ("OSTERGAARD SOREN"/AU OR "OSTERGAARD SOREN"/IN)
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L15 19 SEA FILE=HCAPLUS ABB=ON PLU=ON (L13 AND (ANTIGEN? OR ASSEMBL? OR LPA? OR LIGAND? OR (AMINO(W)ACID? OR AA OR PEPTIDE OR PROTEIN)(W)SYSTEM?)) NOT L14
L16 27 SEA FILE=HCAPLUS ABB=ON PLU=ON ((L7 OR L8) AND (ANTIGEN? OR

ASSEMBL? OR LPA? OR LIGAND? OR (AMINO(W)ACID? OR AA OR PEPTIDE OR PROTEIN)(W)SYSTEM?)) NOT (L10 OR L12 OR L15 OR L14)

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L16 ANSWER 1 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:831539 HCAPLUS
DOCUMENT NUMBER: 134:84820
TITLE: Longer peptide can be accommodated in the MHC class I binding site by a protrusion mechanism
AUTHOR(S): Stryhn, Anette; Pedersen, Lars Ostergaard; **Holm**; **Arne**; Buus, Soren
CORPORATE SOURCE: Institute of Medical Microbiology and Immunology, University of Copenhagen, Copenhagen, Den.
SOURCE: Eur. J. Immunol. (2000), 30(11), 3089-3099
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB According to current consensus, CD8+ T cell responses are focused upon short peptide sequences (8-11 amino acids) presented by MHC class I mols. This size restriction is thought to operate mostly at the level of peptide-MHC class I interaction. Crystal structures have shown that the free N and C termini of a bound peptide interact through hydrogen bonding networks to conserved residues at either end of the class I binding site. Accordingly, it is thought that the termini are fixed and that only minor variations in peptide size are possible through a central bulging mechanism. We find that this consensus view is not always correct as some peptide-MHC class I interaction will accept significant extensions. Furthermore, our results indicate that in some cases protrusion, rather than bulging, may be the mechanism of extension. Depending upon the particular peptide-MHC combination in question, such extensions can occur at either the N or C terminus (but never both at the same time). Finally, we show that MHC and T cell in some cases can detect the identity of the extension, i.e. that extensions may be part of the specificity of the T cell immune response. We suggest that such extensions may play a physiol. role.
REFERENCE COUNT: 28
REFERENCE(S): (1) Bouvier, M; Science 1994, V265, P398 HCAPLUS
(2) Buus, S; Biochim Biophys Acta 1995, V1243, P453 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:514662 HCAPLUS
DOCUMENT NUMBER: 133:172364
TITLE: Neurite outgrowth induced by a synthetic peptide **ligand** of neural cell adhesion molecule requires fibroblast growth factor receptor activation
AUTHOR(S): Ronn, Lars C. B.; Doherty, Patrick; **Holm, Arne**; Berezin, Vladimir; Bock, Elisabeth
CORPORATE SOURCE: The Protein Laboratory, Institute of Molecular Pathology, Panum Institute, Copenhagen, DK-2200, Den.
SOURCE: J. Neurochem. (2000), 75(2), 665-671
CODEN: JONRA9; ISSN: 0022-3042
PUBLISHER: Lippincott Williams & Wilkins

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The neural cell adhesion mol. NCAM is involved in axonal outgrowth and target recognition in the developing nervous system. In vitro, NCAM-NCAM binding has been shown to induce neurite outgrowth, presumably through an activation of fibroblast growth factor receptors (FGFRs). The authors have recently identified a neuritogenic **ligand**, termed the C3 peptide, of the first Ig module of NCAM using a combinatorial library of synthetic peptides. Here the authors investigate whether stimulation of neurite outgrowth by this synthetic **ligand** of NCAM involves FGFRs. In primary cultures of cerebellar neurons from wild-type mice, the C3 peptide stimulated neurite outgrowth. This response was virtually absent in cultures of cerebellar neurons from transgenic mice expressing a dominant-neg. form of the FGFR1. Likewise, in PC12E2 cells transiently expressing a dominant-neg. form of the mouse FGFR1, induction of neurites by the C3 peptide was abrogated. These findings suggest that the neuritogenic effect of the C3 peptide requires the presence of functional FGFRs and support the hypothesis that FGFRs are essential in cell adhesion mol.-stimulated neurite outgrowth. The C3 peptide appears to stimulate neurite outgrowth by specifically activating an NCAM-FGFR-dependent signaling cascade and may therefore be of considerable interest as a tool for the detn. of NCAM-dependent neurite outgrowth as well as a potential drug capable of promoting outgrowth and regeneration of NCAM-responsive axons.
REFERENCE COUNT: 27
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:411590 HCAPLUS
DOCUMENT NUMBER: 133:148866
TITLE: Efficient protection against Mycobacterium tuberculosis by vaccination with a single subdominant epitope from the ESAT-6 **antigen**
AUTHOR(S): Olsen, Anja Weinreich; Hansen, Paul Robert; **Holm, Arne**; Andersen, Peter
CORPORATE SOURCE: Department of TB Immunology, Statens Serum Institute, Copenhagen, Den.
SOURCE: Eur. J. Immunol. (2000), 30(6), 1724-1732
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have investigated the vaccine potential of two peptides derived from the 6-kDa early secretory **antigenic** target (ESAT)-6 **antigen** in the mouse model of tuberculosis. The peptides were both strongly immunogenic in B6CBAF1 (H-2b,k) mice and primed recall responses of the same intensity after immunization. However, both tuberculosis infection and immunization with ESAT-6 resulted in responses focused towards ESAT-61-20. Multiple **antigen** peptide constructs as well as free peptides were emulsified with di-Me dioctadecylammonium bromide/monophosphoryl lipid A/IL-2 and tested as exptl. vaccines in an i.v. and aerosol model of tuberculosis in mice. The peptide were highly immunogenic and induced cellular responses of the same magnitude. However, only vaccines based on the subdominant ESAT-651-70 epitope promoted significant levels of protective immunity and the level of

protection was equiv. to that achieved with ESAT-6 and BCG. These findings demonstrate the potential of peptide-based vaccines against tuberculosis and indicate that there is not direct correlation between the hierarchy of response to naturally processed peptides and their ability to induce protective immunity against Mycobacterium tuberculosis.

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REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 4 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:44892 HCAPLUS
DOCUMENT NUMBER: 133:3434
TITLE: A stem peptide carrier for the immunogenic presentation of peptides
AUTHOR(S): Heegaard, Peter M. H.; Bog, Yang S.; Jakobsen, Palle H.; **Holm, Arne**
CORPORATE SOURCE: Dept. Biochemistry & Immunology, Danish Veterinary Laboratory, Copenhagen, 1790, Den.
SOURCE: Innovation Perspect. Solid Phase Synth. Comb. Libr., Collect. Pap., Int. Symp., 5th (1999), Meeting Date 1997, 143-146. Editor(s): Epton, Roger. Mayflower Scientific Ltd.: Kingswinford, UK.
CODEN: 68OEAA
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The authors have prepd. a simple, short lipopeptide carrier, the stem peptide, which is synthesized by std. Fmoc chem. and used for side-chain presentation of peptides, giving rise to side-chain peptide-specific antibodies by immunization without the inclusion of a carrier protein. The data indicate that even the use of adjuvant may not always be necessary. The stem peptide is an alternative to dendritic peptide carriers, and leads to highly defined, sol. and conformationally stabilized peptide immunogens. Here, to investigate the immunogenicity of the branched constructs, a 21 amino acid malarial peptide from the erythrocyte-binding protein (EBA) involved in erythrocyte invasion was coupled to a stem peptide carrier and then used to immunize mice. Esp. together with Freunds adjuvant, the derivatized carrier induced the prodn. of high levels of branch-peptide specific antibodies after immunization.

REFERENCE COUNT: 7
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 5 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:6214 HCAPLUS
DOCUMENT NUMBER: 132:320872
TITLE: A highly efficient, universal and unbiased approach to address MHC specificity. Quantitation by peptide libraries and improved prediction of binding
AUTHOR(S): Stryhn, A.; Pedersen, L. Ostergaard; Romme, T.; Bisgaard Holm, C.; **Holm, A.**; Buus, S.
CORPORATE SOURCE: Department of Experimental Immunology, University of

Copenhagen, Copenhagen, 2200, Den.
SOURCE: HLA: [Proc. Int. Histocompat. Workshop Conf.], 12th (1997), Meeting Date 1996, Volume 2, 435-438. Editor(s): Charron, Dominique. EDK, Medical and Scientific International Publisher: Sevres, Fr. CODEN: 68MRA5
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Highly efficient, universal and unbiased approach to address MHC specificity by positional scanning combinatorial peptide libraries (PSCPL) was studied. The influenza virus hemagglutinin octamer peptide Ha (255-262) (FESTGNLI) was studied to investigate the specificity of H-2Kk by replacing each aminoacid by other aminoacids. Most of the substitutions had marginal effects on binding except that a replacement, at position 2 and 8 has significant deleterious effects.
REFERENCE COUNT: 10
REFERENCE(S): (1) Babbitt, B; Nature 1985, V317, P359 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 6 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:629645 HCAPLUS
DOCUMENT NUMBER: 132:1371
TITLE: Predicting Binding Affinities of Protein **Ligands** from Three-Dimensional Models: Application to Peptide Binding to Class I Major Histocompatibility Proteins
AUTHOR(S): Rognan, Didier; Lauemoller, Sanne Lise; **Holm, Arne**; Buus, Soren; Tschinke, Vincenzo
CORPORATE SOURCE: Department of Pharmacy, Swiss Federal Institute of Technology, Zurich, CH-8057, Switz.
SOURCE: J. Med. Chem. (1999), 42(22), 4650-4658 CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A simple and fast free energy scoring function (Fresno) has been developed to predict the binding free energy of peptides to class I major histocompatibility (MHC) proteins. It differs from existing scoring functions mainly by the explicit treatment of **ligand** desolvation and of unfavorable protein-**ligand** contacts. Thus, it may be particularly useful in predicting binding affinities from three-dimensional models of protein-**ligand** complexes. The Fresno function was independently calibrated for two different training sets: (a) five HLA-A*0201-peptide structures, which had been detd. by X-ray crystallog., and (b) three-dimensional models of 37 H-2Kk-peptide structures, which had been obtained by knowledge-based homol. modeling. For both training sets, a good cross-validated fit to exptl. binding free energies was obtained with predictive errors of 3-3.5 kJ/mol. As expected, lipophilic interactions were found to contribute the most to HLA-A*0201-peptide interactions, whereas H-bonding predominates in H-2Kk recognition. Both cross-validated models were afterward used to predict the binding affinity of a test set of 26 peptides to HLA-A*0204 (an HLA allele closely related to HLA-A*0201) and of a series of 16 peptides to H-2Kk. Predictions were more accurate for HLA-A2-binding peptides as the training set had been built from exptl. detd. structures. The av. error in predicting the binding free energy of the test peptides was 3.1 kJ/mol. For the homol. model-derived equation, the av. error in predicting the binding free energy of peptides to Kk was significantly higher (5.4

kJ/mol) but still very acceptable. The present scoring function is thus able to predict with a good accuracy binding free energies from three-dimensional models, at the condition that the backbone coordinates of the MHC-bound peptide have first been detd. with an accuracy of about 1-1.5 .ANG.. Furthermore, it may be easily re-calibrated for any protein-**ligand** complex.

REFERENCE COUNT: 67
REFERENCE(S):
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 7 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:186738 HCAPLUS
DOCUMENT NUMBER: 131:30773
TITLE: Human T cell responses to the ESAT-6 **antigen** from Mycobacterium tuberculosis
AUTHOR(S): Ravn, Pernille; Demissie, Abebech; Eguale, Tewodros; Wondwosson, Hailu; Lein, David; Amoudy, Hanady A.; Mustafa, Abu S.; Jensen, Axel Kok; **Holm, Arne** ; Rosenkrands, Ida; Oftung, Fredrik; Olobo, Joseph; Von Reyn, Fordham; Andersen, Peter
CORPORATE SOURCE: Department of Tuberculosis Immunology, Statens Seruminstitut, Department of Pulmonary Medicine, Rigshospitalet, Royal Veterinary and Agricultural University, Copenhagen, Den.
SOURCE: J. Infect. Dis. (1999), 179(3), 637-645
CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER: University of Chicago Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Human T cell responses to ESAT-6 and eight synthetic overlapping peptides were investigated in tuberculosis (TB) patients and control subjects from regions of high and low endemicity for TB. ESAT-6 was recognized by 65% of all tuberculin purified protein deriv.-responsive TB patients, whereas only 2 of 29 bacille Calmette-Guerin-vaccinated Danish healthy donors recognized this mol. In Ethiopia, a high frequency (58%) of healthy contacts of TB patients recognized ESAT-6. All of the peptides were recognized by some donors, indicating that the mol. holds multiple epitopes. Danish and Ethiopian patients differed in the fine specificity of their peptide responses. Recognition of the C-terminal region (aa 72-95) was predominant in Danish patients, whereas recognition of aa 42-75 was predominant in Ethiopia. The relationship of these differences to the distribution of HLA types in the two populations is discussed. This study demonstrates that ESAT-6 is frequently recognized during early infection and holds potential as a component of a future TB-specific diagnostic reagent.

REFERENCE COUNT: 47
REFERENCE(S):
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(2) Andersen, P; J Immunol 1995, V154, P3359 HCAPLUS
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(5) Brandt, L; J Immunol 1996, V157, P3527 HCAPLUS
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ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 8 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:551331 HCAPLUS
DOCUMENT NUMBER: 129:259126
TITLE: The P9 pocket of HLA-DQ2 (non-Asp.beta.57) has no particular preference for negatively charged anchor

residues found in other type 1 diabetes-predisposing non-Asp.beta.57 MHC class II molecules
AUTHOR(S): Quarsten, Hanne; Paulsen, Gunnar; Johansen, Bente H.; Thorpe, Christopher J.; **Holm, Arne**; Buus, Soren; Solid, Ludvig M.
CORPORATE SOURCE: Inst. of Transplantation Immunology, Rikshospitalet, Univ. of Oslo, Oslo, 0027, Norway
SOURCE: Int. Immunol. (1998), 10(8), 1229-1236
CODEN: INIMEN; ISSN: 0953-8178
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Susceptibility and resistance to type 1 diabetes are assocd. with MHC class II alleles that carry non-Asp and Asp at residue 57 of their .beta. chain resp. The effect of Asp or non-Asp.beta.57 may relate to a differential ability of distinct class II mols. to bind specific immuno-pathogenic peptides. Recent studies in man and mouse have revealed that some type 1 diabetes-predisposing non-Asp.beta.57 class II mols. (i.e. DQ8, DR4Dw15 and I-Ag7) preferentially bind peptides with a neg. charged anchor residue at P9. It has been suggested that this is a common feature of type 1 diabetes-predisposing class II mols. The mol. explanation for such a phenomenon could be that class II .beta. chains with ASp.beta.57 form a salt bridge between Asp.beta.57 and a conserved Arg of the .alpha. chain, whereas in non-Asp.beta.57 mols. the Arg is unopposed and free to interact with neg. charged P9 peptide anchor residues. The authors have investigated the specificity of the P9 pocket of the type 1 diabetes-assocd. DQ2 mol. and in particular examd. for charge effects at this anchor position. Different approaches were undertaken. The authors analyzed binding of a high-affinity binding **ligand** and P9-substituted variants of this peptide, and the authors analyzed the binding of a set of synthetic random peptide libraries. The binding analyses were performed with wild-type DQ2 and a mutated DQ2 with Ala at .beta.57 substituted with Asp. The authors' results indicate that the wild-type DQ2 (non-Asp.beta.57) prefers large hydrophobic residues at P9 and that there is no particular preference for binding peptides with neg. charged residues at this position. The specificity of the P9 pocket in the mutated DQ mol. is altered, indicating that the .beta.57 residue contributes to detg. the specificity of the P9 pocket. The data do not lend support to the hypothesis that all non-Asp .beta.57 class II mols. predispose to development of disease by binding peptides with neg. charged P9 anchor residues.

L16 ANSWER 9 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:67789 HCAPLUS
DOCUMENT NUMBER: 128:179092
TITLE: B-cell epitopes and quantification of the ESAT-6 protein of Mycobacterium tuberculosis
AUTHOR(S): Harboe, Morten; Malin, Adam S.; Dockrell, Hazel S.; Wiker, Harald Gotten; Ulvund, Gunni; **Holm, Arne**; Jorgensen, Mikala Clok; Andersen, Peter
CORPORATE SOURCE: Institute of Immunology and Rheumatology, University of Oslo, Oslo, N-0172, Norway
SOURCE: Infect. Immun. (1998), 66(2), 717-723
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB ESAT-6 is an important T-cell **antigen** recognized by protective T cells in animal models of infection with Mycobacterium tuberculosis. In an ELISA with overlapping peptides spanning the sequence of ESAT-6, monoclonal antibody HYB76-8 reacted with two peptides in the N-terminal region of the mol. Assays with synthetic truncated peptides allowed a precise mapping of the epitope to the residues EQQWNFAGIEAAA at positions

3 to 15. Hydrophilicity plots revealed one hydrophilic area at the N terminus and two addnl. areas further along the polypeptide chain. Antipeptide antibodies were generated by immunization with synthetic 8-mer peptides corresponding to these two regions coupled to keyhole limpet hemocyanin. Prolonged immunization with a 23-mer peptide (positions 40 to 62) resulted in the formation of antibodies reacting with the peptide as well as native ESAT-6. A double-antibody ELISA was then developed with monoclonal antibody HYB76-8 as a capture antibody, **antigen** for testing in the second layer, and antipeptide antibody in the third layer. The assay was suitable for quantification of ESAT-6 in M. tuberculosis **antigen** prepns., showing no reactivity with M. bovis BCG Tokyo culture fluid, used as a neg. control, or with MPT64 or **antigen** 85B, previously shown to cross-react with HYB76-8. This capture ELISA permitted the identification of ESAT-6 expression from vaccinia virus constructs contg. the esat-6 gene; this expression could not be identified by std. immunoblotting.

L16 ANSWER 10 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:472462 HCAPLUS
DOCUMENT NUMBER: 127:160185
TITLE: MHC class I binding motifs: an unbiased quantitative approach to motif definition
AUTHOR(S): Stryhn, Anette; Pedersen, Lars Oestegaard; Romme, Tina; Holm, Charlotte Bisgaard; **Holm, Arne**; Buus, Soeren
CORPORATE SOURCE: Institute of Medical Microbiology and Immunology, University of Copenhagen, Copenhagen, Den.
SOURCE: Alfred Benzon Symp. (1997), 40(HLA and Disease: The Molecular Basis), 133-147
CODEN: ABSYB2; ISSN: 0105-3639
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion, with 40 refs., on MHC restriction, MHC polymorphism, MHC specificity, motif identification, hemagglutinin peptide 255-262 binding to Kk, positional scanning combinatorial peptide libraries (PSCPL), predictions based on the PSCPL approach, and complete mapping of all human MHC specificities.

L16 ANSWER 11 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1997:364667 HCAPLUS
DOCUMENT NUMBER: 127:32565
TITLE: Characterization of the delayed type hypersensitivity-inducing epitope of MPT64 from Mycobacterium tuberculosis
AUTHOR(S): Oettinger, T.; **Holm, A.**; Hasloev, K.
CORPORATE SOURCE: TB Research Unit, Department of Mycobacteriology, Statens Serum Institut, Copenhagen, DK-2300, Den.
SOURCE: Scand. J. Immunol. (1997), 45(5), 499-503
CODEN: SJIMAX; ISSN: 0300-9475
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mycobacterium tuberculosis secretes several proteins into the extracellular environment, some of which are restricted to the M. tuberculosis complex. One of these **antigens** is MPT64. Recently, the authors showed that native as well as recombinant MPT64 is able to distinguish between an M. tuberculosis infection and a BCG Danish 1331 vaccination. Improved distinction between tuberculin purified protein deriv. (PPD) sensitivity conferred by an M. tuberculosis infection and that induced by a BCG vaccination or infection with environmental mycobacteria would be useful in the control of tuberculosis. In this study, the authors report the mapping and characterization of a

Dth-inducing epitope by the use of synthetic peptides in guinea-pigs vaccinated with BCG Danish 1331 or Tokyo. Studies with overlapping synthetic peptides have pinpointed the biol. activity to a single Dth-inducing epitope at the C-terminal region of MPT64 consisting of 15 residues between amino acids Gly-173 and Ala-187, the core epitope (CE15). A fine mapping using truncated versions of CE15 indicates the epitope is restricted to 13 residues between amino acids Val-174 to Glu-186. However, the optimal Dth reactivity is obtained by CE15. Different modifications of CE15 revealed that a lysine tree construction improves the skin reactivity to a max. level approaching that of the reactivity to tuberculin PPD.

L16 ANSWER 12 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:632476 HCAPLUS
DOCUMENT NUMBER: 125:325659
TITLE: Key epitopes on the ESAT-6 **antigen** recognized in mice during the recall of protective immunity to Mycobacterium tuberculosis
AUTHOR(S): Brandt, Lise; Oettinger, Thomas; **Holm, Arne**; Andersen, Aase B.; Andersen, Peter
CORPORATE SOURCE: Bacterial Vaccine and Mycobacteria Dep., Royal Veterinary and Agricultural Univ., Copenhagen, Den.
SOURCE: J. Immunol. (1996), 157(8), 3527-3533
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The recall of long-lived immunity in a mouse model of tuberculosis (TB) is defined as an accelerated accumulation of reactive T cells in the target organs. The authors have recently identified **antigen** (Ag) 85B and a 6-kDa early secretory **antigenic** target, designated ESAT-6, as key **antigenic** targets recognized by these cells. Here, preferential recognition of the ESAT-6 Ag during the recall of immunity was shared by 5 of 6 genetically different strains of mice. Overlapping peptides spanning the sequence of ESAT-6 were used to map 2 T cell epitopes on this mol. One epitope recognized in the context of H-2b,d was located in the N-terminal part of the mol., whereas an epitope recognized in the context of H-2a,k covered amino acids 51-60. Shorter versions of the N-terminal epitope allowed the precise definition of a 13-amino acid core sequence recognized in the context of H-2b. The peptide covering the N-terminal epitope was immunogenic, and a T cell response with the same fine specificity as that induced during TB infection was generated by immunization with the peptide in IFA. In the C57BL/6j strain, this single epitope was recognized by an exceedingly high frequency of splenic T cells (.apprx.1:1000), representing 25-35% of the total culture filtrate-reactive T cells recruited to the site of infection during the first phase of the recall response. These findings emphasize the relevance of this Ag in the immune response to TB and suggest that immunol. recognition in the first phase of infection is a highly restricted event dominated by a limited no. of T cell clones.

L16 ANSWER 13 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:575785 HCAPLUS
DOCUMENT NUMBER: 125:219078
TITLE: Shared fine specificity between T-cell receptors and an antibody recognizing a peptide/major histocompatibility class I complex
AUTHOR(S): Stryhn, Anette; Andersen, Peter S.; Pedersen, Lars Oe.; Svejgaard, Arne; **Holm, Arne**; Thorpe, Christopher J.; Fugger, Lars; Buus, Soeren; Engberg, Jan
CORPORATE SOURCE: Institute Medical Microbiol. and Immunology, Univ. Copenhagen, Copenhagen, Den.
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1996), 93(19),

10338-10342
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cytotoxic T cells recognize mosaic structures consisting of target peptides embedded within self-major histocompatibility complex (MHC) class I mols. This structure has been described in great detail for several peptide-MHC complexes. In contrast, how T-cell receptors recognize peptide-MHC complexes have been less well characterized. We have used a complete set of singly substituted analogs of a mouse MHC class I, Kk-restricted peptide, influenza hemagglutinin (Ha)255-262, to address the binding specificity of this MHC mol. Using the same peptide-MHC complexes we detd. the fine specificity of two Ha255-262-specific, Kk-restricted T cells, and of a unique antibody, pSAN, specific for the same peptide-MHC complex. Independently, a model of the Ha255-262-Kk complex was generated through homol. modeling and mol. mechanics refinement. The functional data and the model corroborated each other showing that peptide residues 1, 3, 4, 6, and 7 were exposed on the MHC surface and recognized by the T cells. Thus, the majority, and perhaps all, of the side chains of the non-primary anchor residues may be available for T-cell recognition, and contribute to the stringent specificity of T cells. A striking similarity between the specificity of the T cells and that of the pSAN antibody was found and most of the peptide residues, which could be recognized by the T cells, could also be recognized by the antibody.

L16 ANSWER 14 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:487229 HCAPLUS
DOCUMENT NUMBER: 125:165268
TITLE: Peptide binding specificity of major histocompatibility complex class I resolved into an array of apparently independent subspecificities: quantification by peptide libraries and improved prediction of binding
AUTHOR(S): Stryhn, Anette; Pedersen, Lars Oestegaard; Romme, Tina; Holm, Charlotte Bisgaard; **Holm, Arne**; Buus, Soeren
CORPORATE SOURCE: Inst. Medical Microbiology, Univ. Copenhagen, Copenhagen, DK-2200, Den.
SOURCE: Eur. J. Immunol. (1996), 26(8), 1911-1918
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Considerable interest has focused on understanding how major histocompatibility complex (MHC) specificity is generated and characterizing the specificity of MHC mols. with the ultimate goal being to predict peptide binding. We have used a strategy where all possible peptides of a particular size are distributed into positional scanning combinatorial peptide libraries (PSCPL) to develop a highly efficient, universal and unbiased approach to address MHC specificity. The PSCPL approach appeared qual. and quant. superior to other currently used strategies. The av. effect of any amino acid in each position was quantitated, allowing a detailed description of extended peptide binding motifs including primary and secondary anchor residues. It also identified disfavored residues which were found to be surprisingly important in shaping MHC class I specificity. Assuming that MHC class I specificity is the result of largely independently acting subsites, the binding of unknown peptides could be predicted. Conversely, this argues that MHC class I specificities consist of an array of subspecificities acting in a combinatorial mode.

L16 ANSWER 15 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:129630 HCAPLUS
DOCUMENT NUMBER: 124:172920

TITLE: Characterization of two conformational epitopes of the Chlamydia trachomatis serovar L2 DnaK immunogen
AUTHOR(S): Birkellund, Svend; Mygind, Per; **Holm, Arne**; Larsen, Bente; Beck, Frederik; Christiansen, Gunna
CORPORATE SOURCE: Dep. of Medical Microbiology and Immunology, Univ. of Aarhus, Aarhus, DK-8000, Den.
SOURCE: Infect. Immun. (1996), 64(3), 810-17
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Chlamydia trachomatis DnaK is an important immunogen in chlamydial infections. DnaK is composed of a conserved N-terminal ATP-binding domain and a variable C-terminal peptide-binding domain. To locate the immunogenic part of C. trachomatis DnaK, we generated monoclonal antibodies (MAbs) against this protein. By use of recombinant DNA techniques, we located the epitopes for two MAbs in the C-terminal variable part. Although the antibodies reacted in an immunoblot assay, it was not possible to map the epitopes completely by use of 16-mer synthetic peptides displaced by one amino acid corresponding to the C-terminal part of C. trachomatis DnaK. To det. the limits of the epitopes, C. trachomatis DnaK and glutathione S-transferase fusion proteins were constructed and affinity purified. The purified DnaK fusion proteins were used for a fluid-phase inhibition ELISA with the two antibodies. The epitopes were found not to overlap. To obtain DnaK fragments recognized by the antibodies with the same affinity as native C. trachomatis DnaK, it was necessary to express, resp., regions of 127 and 77 amino acids. The MAbs described in this study thus recognized conformational epitopes of C. trachomatis DnaK.

L16 ANSWER 16 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:99500 HCAPLUS
DOCUMENT NUMBER: 124:140406
TITLE: Combinatorial peptide library and method
INVENTOR(S): Hodges, Robert S.; Irvin, Randall T.; **Holm, Arne**; Wong, Wah Y.; Sheth, Hasmukh B.; Husband, Devon L.
PATENT ASSIGNEE(S): S.P.I. Synthetic Peptides Inc., Can.
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9534575	A1	19951221	WO 1995-IB560	19950613
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5738996	A	19980414	US 1994-260199	19940615
AU 9528059	A1	19960105	AU 1995-28059	19950613

PRIORITY APPLN. INFO.: US 1994-260199 A 19940615
WO 1995-IB560 W 19950613

AB A combinatorial library compn. and method for using the library to construct oligomers effective to bind to a selected **ligand** is disclosed. The library compn. includes at least two sets of combinatorial oligomer libraries, each library set having selected oligomer subunit positions filled by known subunits, and other subunit positions contg. permutations of subunits. In the selection method, oligomers from each library set are identified, and a new permutation library formed of subunits corresponding to the highest binding affinity oligomers in each library is screened for binding affinity to the selected **ligand**.

L16 ANSWER 17 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:974613 HCAPLUS
DOCUMENT NUMBER: 124:53598
TITLE: Mapping of the delayed-type hypersensitivity-inducing epitope of secreted protein MPT64 from Mycobacterium tuberculosis
AUTHOR(S): Oettinger, Thomas; **Holm, Arne**; Mtoni, Isaac M.; Andersen, Aase B.; Kasloev, Kaare
CORPORATE SOURCE: Mycobacteria Dept., Statens Seruminstitut, Copenhagen, DK-2300, Den.
SOURCE: Infect. Immun. (1995), 63(12), 4613-18
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The gene encoding the immunogenic protein MPT64 found in culture filtrates of Mycobacterium tuberculosis H37Rv was expressed in Escherichia coli K-12 and purified as a recombinant protein. The purified recombinant MPT64 elicited delayed-type hypersensitivity (DTH) in outbred guinea pigs sensitized with Mycobacterium bovis BCG Tokyo. The skin reactions were comparable to those obtained with native MPT64. No skin reactions were obsd. when either recombinant MPT64 or native MPT64 was used in guinea pigs sensitized with M. bovis BCG Danish 1331. Amino- and carboxy-terminal deletion mutants of MPT64 were purified as fusion proteins for the mapping of DTH-inducing epitopes on recombinant MPT64 by use of the guinea pig skin test model. The part of the mol. responsible for the biol. activity was located at the carboxy-terminal end. Further studies with overlapping synthetic peptides have pinpointed the biol. activity at a single DTH-inducing epitope consisting of 15 residues between amino acids Gly-173 and Ala-187. Screening by PCR of 56 clin. isolates of M. tuberculosis from Danish and Tanzanian patients demonstrated the presence of mpt64 in all of the strains. These results point to MPT64 as a possible candidate for a skin test reagent specific for diagnosis of human tuberculosis.

L16 ANSWER 18 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:678371 HCAPLUS
DOCUMENT NUMBER: 121:278371
TITLE: Characterization of a linear epitope on Chlamydia trachomatis serovar L2 DnaK-like protein
AUTHOR(S): Birkelund, Svend; Larsen, Bente; **Holm, Arne**; Lundemose, Anker G.; Christiansen, Gunna
CORPORATE SOURCE: Inst. Med. Microbiol., Univ. Aarhus, Aarhus, DK-8000, Den.
SOURCE: Infect. Immun. (1994), 62(5), 2051-7
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A cytoplasmic 75-kDa immunogen from Chlamydia trachomatis serovar L2 has previously been characterized as being similar to the Escherichia coli heat shock protein DnaK. We have localized a linear epitope for one monoclonal antibody specific for C. trachomatis DnaK. By use of a recombinant DNA technique, the epitope was limited to 14 amino acids. With synthetic peptides, the epitope was further limited to eight amino acids. Six of these amino acids are conserved in bovine HSP70, which has a known three-dimensional structure. The amino acid sequence homologous to the epitope is located in a linear part of the HSP70 mol. known as connect II.

L16 ANSWER 19 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:677739 HCAPLUS
DOCUMENT NUMBER: 121:277739
TITLE: A cleaved form of the receptor for urokinase-type plasminogen activator in invasive transplanted human

and murine tumors
AUTHOR(S): Solberg, Helene; Roemer, John; Brunner, Nils; **Holm, Arne**; Sidenius, Nicolai; Danoe, Keld; Hoeyer-Hansen, Gunilla
CORPORATE SOURCE: Finsen Laboratory, Rigshospitalet, Copenhagen, DK-2100, Den.
SOURCE: Int. J. Cancer (1994), 58(6), 877-81
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was recently found that urokinase-type plasminogen activator (uPA) is involved in the cleavage of its receptor (uPAR) on cultured cells, thereby releasing one of the receptor's 3 domains (the **ligand** binding domain 1) and leaving the 2 others [uPAR(2 + 3)] anchored to the cell surface. With monoclonal antibodies (MAbs) we have now identified human uPAR(2 + 3) in lysates of invasive human MDA-MB-231 mammary carcinomas xenografted into nude mice. The prodn. of peptide antibodies recognizing different domains of murine uPAR made it possible to identify a similar cleaved form of uPAR, murine uPAR(2 + 3), in exts. of primary Lewis lung carcinomas. Cleavage of uPAR also occurs in cultured MDA-MB-231 cells and Lewis lung carcinoma cells. This cleavage is inhibited by anticatalytic antibodies to either human or murine uPA, resp., indicating that it is catalyzed by either uPA or plasmin generated by uPA. The amt. of uPAR(2 + 3) may therefore be directly related to the activity of the uPA system and it is possible that the level of uPAR(2 + 3) in cancer tissue may prove to be a stronger prognostic parameter than the levels of either full-length uPAR or UPA.

L16 ANSWER 20 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:241931 HCAPLUS
DOCUMENT NUMBER: 120:241931
TITLE: A quantitative assay to measure the interaction between immunogenic peptides and purified class I major histocompatibility complex molecules
AUTHOR(S): Olsen, Anna Catharina; Pedersen, Lars Oestergaard; Hansen, Anette Stryhn; Nissen, Mogens Holst; Olsen, Marianne; Hansen, Paul Robert; **Holm, Arne**; Buus, Soeren
CORPORATE SOURCE: Med. Fac., Univ. Copenhagen, Copenhagen, DK-2200, Den.
SOURCE: Eur. J. Immunol. (1994), 24(2), 385-92
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A direct and sensitive biochem. assay to measure the interaction in soln. between peptides and affinity-purified major histocompatibility complex (MHC) class I mols. has been generated. Specific binding reflecting the known class I restriction of cytotoxic T cells responses was obtained. Adding an excess of .beta.2-microglobulin (.beta.2m) significantly increased the rate of peptide assocn., but it did not affect the rate of dissocn. Binding was complicated by a rapid and apparently irreversible loss of functional MHC class I at 37.degree.C which might limit the life span of empty MHC class I, thereby preventing the inadvertent exchange of peptides at the target cell surface. All class I mols. tested bound peptides of the canonical octameric to nonameric length. However, one class I mol., Kk, also bound peptides which were much longer, suggesting that the preference of class I mols. for short epitopes is not abs. and may be caused by factors other than the peptide-MHC class I binding event itself.

L16 ANSWER 21 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:49430 HCAPLUS
DOCUMENT NUMBER: 120:49430
TITLE: Peptide dot immunoassay and immunoblotting:

electroblotting from aluminum thin-layer chromatography plates and isoelectric focusing gels to activated nitrocellulose
AUTHOR(S): Lauritzen, Edgar; Masson, Mar; Rubin, Inger; Bjerrum, Ole J.; **Holm, Arne**
CORPORATE SOURCE: Dep. Virol., Statens Seruminst., Copenhagen, DK-2300, Den.
SOURCE: Electrophoresis (Weinheim, Fed. Repub. Ger.) (1993), 14(9), 852-9
CODEN: ELCTDN; ISSN: 0173-0835
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nitrocellulose membrane was preactivated with divinyl sulfone, and a spacer of 1,6-diaminohexane was coupled to the membrane which was functionalized by glutaraldehyde, leaving a reactive carbonyl group. The peptides were coupled to the carbonyl by the side chain and terminal amino groups. The octa-peptide angiotensin II (sequence: DRVYIHPF) and peptide analogs contg. 6-10 amino acid residues were dotted directly onto the matrix at 45.degree. for 15 min and detected by specific antisera, which were raised in rabbits against angiotensin I and II, resp. They were visualized by peroxidase-coupled anti-rabbit IgG antibodies. The detection limit for synthetic angiotensin II was 500 fg per cm2 (= 500 amol per cm2) and for the decapeptide angiotensin I (sequence: DRVYIHPFHL) it was 500 pg per cm2 (= 400 fmol per cm2). Sepn. of synthetic angiotensin analogs by high performance thin-layer chromatog. on silica coated aluminum plates was followed by electroblotting onto activated nitrocellulose and detection with specific antibodies, showing a sensitivity of 100 fg and 1 pg for angiotensin II and angiotensin I, resp. Isoelec. focusing in agarose using Ampholine carrier ampholytes and immunoblotting with specific antisera displayed a lower sensitivity for angiotensin II and angiotensin 1 of 2 ng and 20 ng, resp. The isoelec. focusing and immunoblotting technique was applied for sepn. of angiotensin I and II and related peptides in serum, where synthetic angiotensin I was degraded in the presence of 1 mM phenylmethylsulfonyl fluoride and 10 mM EDTA. The versatility of dot immunobinding on activated nitrocellulose was shown with two sera from patients infected with human immunodeficiency virus, HIV-1 and HIV-2, by using pH 10.2 in incubation media, resulting in a low background. These sera were bound specifically to either one of the closely related HIV-1 and HIV-2 peptide **antigens** from the two viruses.

L16 ANSWER 22 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:6323 HCAPLUS
DOCUMENT NUMBER: 120:6323
TITLE: Chemical activation of nitrocellulose membranes for peptide **antigen**-antibody binding studies: direct substitution of the nitrate group with diaminoalkane
AUTHOR(S): Masson, Mar; Lauritzen, Edgar; **Holm, Arne**
CORPORATE SOURCE: H.C Inst., Univ. Copenhagen, Copenhagen, Den.
SOURCE: Electrophoresis (Weinheim, Fed. Repub. Ger.) (1993), 14(9), 860-5
CODEN: ELCTDN; ISSN: 0173-0835
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A method to covalently link peptide and proteins, through a diaminoalkane spacer to nitrocellulose membrane was developed for immunochem. applications. Initially the nitrocellulose membrane was modified by covalent incorporation of diaminoalkane spacers without any prior activation. The incorporation was shown primarily to involve .alpha.-elimination of the nitrate groups, and an imine was formed between the carbonyl group on the membrane and the diaminoalkane. The rate of incorporation increased exponentially with the length of the diaminoalkane

as detd. by a ninhydrin colorimetric reaction, which was developed for the study. More than 200 nmole diamine per mg nitrocellulose could be incorporated, but less than 11 nmol/mg (63 nmol/cm2) was chosen in order to retain the strength of the membrane. The primary amino groups of the modified membrane was glutaraldehyde activated and the octapeptide, angiotensin II, was covalently bound. A dot immunoassay was performed where specific anti-angiotensin II antibodies reacted with the peptide and was visualized by peroxidase coupled secondary antibodies. The results were quantified by video densitometry above 0.005 .mu.g AII per cm2. The immunoassay showed improved detection of the peptide on the activated as compared to unactivated membrane as well as increased retention of radiolabeled [125]angiotensin II.

L16 ANSWER 23 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:99951 HCAPLUS
DOCUMENT NUMBER: 118:99951
TITLE: Identification of murine T-cell epitopes on the S4 subunit of pertussis toxin
AUTHOR(S): Petersen, Jesper W.; **Holm, Arne**; Ibsen, Per H.; Hasloev, Kaare; Heron, Iver
CORPORATE SOURCE: Res. Cnet. Med. Biotechnol., Statens Seruminst., Copenhagen, DK-2300, Den.
SOURCE: Infect. Immun. (1993), 61(1), 56-63
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of the present study was to identify murine T-cell epitopes on pertussis toxin subunit S4. Six mouse strains with 5 different haplotypes at the H-2 locus were immunized with the pertussis toxin B oligomer. Lymph node lymphocytes were isolated and stimulated in an in vitro proliferation assay with pertussis toxin components and 11 overlapping synthetic peptides synthesized on the basis of the primary sequence of S4. In vitro proliferative responses to the synthetic peptides revealed the presence of 4 distinct murine T-cell epitopes on subunit S4. The recognition of the peptides was major histocompatibility complex-restricted. Immunizing 4 of the 6 mouse strains with the synthetic peptides showed that the peptides which were demonstrated to contain T-cell epitopes following immunization with the B oligomer were able to induce proliferative responses to detoxified pertussis toxin and pertussis toxin components contg. subunit S4. One of the identified murine T-cell epitopes corresponded to one of the major human T-cell epitopes previously identified on subunit S4. It is hoped that this murine model system will facilitate the development of a synthetic immunogen mimicking the protective properties of pertussis toxin.

L16 ANSWER 24 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1992:6957 HCAPLUS
DOCUMENT NUMBER: 116:6957
TITLE: Solid phase peptide synthesis of selectively phosphorylated peptides
AUTHOR(S): Staerkaer, Gunnar; Jakobsen, Mogens H.; Olsen, Carl Erik; **Holm, Arne**
CORPORATE SOURCE: H. C. Oersted Inst., Univ. Copenhagen, Copenhagen, DK-2100, Den.
SOURCE: Tetrahedron Lett. (1991), 32(39), 5389-92
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An efficient, selective, solid-phase synthesis of phosphopeptides contg. a multiplicity of hydroxy-contg. amino acids is described. The peptide was **assembled** on the solid support using 9-fluorenymethoxycarbonyl (Fmoc) amino acid active esters without side-chain protection for serine and tyrosine. Phosphorylation was carried out with Et2NP(OCMe3)2 and

1H-tetrazole, followed by oxidn. with Me3COOH. After simultaneous deprotection and cleavage, the phosphopeptide H-Ala-Tyr(PO3H2)-Ala-Ser(PO3H2)-Ala-OH was obtained in high yield with >90% phosphorylation on both residues.

L16 ANSWER 25 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:78092 HCAPLUS
DOCUMENT NUMBER: 114:78092
TITLE: Covalently linked peptides for enzyme-linked immunosorbent assay
AUTHOR(S): Soendergaard-Andersen, Jan; Lauritzen, Edgar; Lind, Klaus; **Holm, Arne**
CORPORATE SOURCE: Res. Cent. Med. Biotechnol., Statens Seruminst., Copenhagen, DK-2300, Den.
SOURCE: J. Immunol. Methods (1990), 131(1), 99-104
CODEN: JIMMBG; ISSN: 0022-1759
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A general method is described, by which synthetic peptides are covalently linked via their carboxyl group to microtiter plates (CovaLink) for ELISA. Peptides were coupled to the microtiter plates using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide and N-hydroxysuccinimide. Plates were prepd. by this method with an angiotensin II peptide and with an HIV-2 peptide and attachment detected by rabbit anti-angiotensin serum and with a pos. serum from an HIV-2-infected patient, resp., using the common ELISA procedure in the last steps. The method is simple to perform, it constitutes an alternative to the common ELISA method, and eliminates the risk of inadvertent loss of peptide during the procedure. The method is highly reproducible and has a high sensitivity. It may be used for either **antigen** or antibody detection.

L16 ANSWER 26 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1991:17616 HCAPLUS
DOCUMENT NUMBER: 114:17616
TITLE: Dot immunobinding and immunoblotting of picogram and nanogram quantities of small peptides on activated nitrocellulose
AUTHOR(S): Lauritzen, Edgar; Masson, Mar; Rubin, Inger; **Holm, Arne**
CORPORATE SOURCE: Virol. Dep., Statens Seruminst., Copenhagen, DK-2300, Den.
SOURCE: J. Immunol. Methods (1990), 131(2), 257-67
CODEN: JIMMBG; ISSN: 0022-1759
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Nitrocellulose was activated with divinyl sulfone, a spacer of ethylenediamine, and glutaraldehyde. The aldehyde groups on the activated nitrocellulose, Nit-CHO, were stable through 1 mo at 4.degree.. Peptides were attached to the membrane by reaction of the amino group with the free carbonyl, forming peptide bonds. The decapeptide angiotensin I (AI), the octapeptide angiotensin II (AII), angiotensin analogs, and Met- and Leu-enkephalin (Met-E and Leu-E) were tested on the membranes with specific rabbit antibodies (sRaAb) against the peptides, and visualized by horseradish peroxidase conjugated anti-rabbit antibody (HRP-anti-RaAb). With this technique AI and AII could be detected with sensitivities of 500 pg/cm2 and 20 pg/cm2, resp. Substitution of Ala7 for Pro7 in AI and AII caused a reduced binding of anti-AI and anti-AII antisera, resp., and it completely abolished crossreactivity of anti-AI with Ala7-AII as well as of anti-AII with Ala7-AI. Peptides from the gp41 and gp36 **antigens** corresponding to the sequence aa596-618 of the human immunodeficiency viruses type 1 and 2, HIV-1 and HIV-2, were tested on Nit-CHO with 2 human sera from infected patients. The serol. reactions were specific for both the HIV-1 and HIV-2 peptide, resp. This indicated

that the technique could be exploited for serol. testing of humans. Sepn. of peptides by high performance thin layer chromatog. (HPTLC) and identification by immunoblotting was demonstrated with angiotensin analogs. After sepn. by HPTLC on silica aluminum plates the peptides were electrotransferred by semidry electroblotting on Nit-CHO, followed by specific antibody overlays and developed as for the dot immunobinding technique. This combined method enabled differentiation between closely related peptide analogs and it improved the sensitivity of peptide detection 100-1000 fold as compared to visualization by quenched fluorescence on chromatog. plates.

L16 ANSWER 27 OF 27 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1990:176538 HCAPLUS
DOCUMENT NUMBER: 112:176538
TITLE: The T-lymphocyte proliferative response to synthetic peptide **antigens** of defined secondary structure
AUTHOR(S): Mouritsen, Soeren; Meldal, M.; Rubin, B.; **Holm, A.**; Werdelin, O.
CORPORATE SOURCE: Inst. Exp. Immunol., Univ. Copenhagen, Copenhagen, DK-2100, Den.
SOURCE: Scand. J. Immunol. (1989), 30(6), 723-30
CODEN: SJIMAX; ISSN: 0300-9475
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Immunodominant sites in proteins recognized by T lymphocytes are segments consisting of at least 7-8 amino acids. It has previously been proposed that these sites in proteins are .alpha.-helical and amphipathic structures. Here, the authors synthesized and investigated the immunogenicity of three synthetic peptides (MP7, MP8, and MP9), each consisting of the same 15 amino acids, but differing with respect to sequence. Based on information anal. and CD measurements, MP7 has an .alpha.-helical secondary structure and based on previously assigned hydrophilicity indexes, was also strongly longitudinally amphiphatic. MP8 also was conformed as an .alpha.-helix, but was amphipathic in the sense that the N-terminal half of the mol. was hydrophilic and the C-terminal half hydrophobic. MP9 had neither an amphipathic nor an .alpha.-helical structure. All three peptides were immunogenic in some strains of mice but none was immunogenic in all strains. This supports other studies concluding that amphipathicity per se is neither a necessary nor sufficient requirement for immunogenicity of a peptide. However, these data suggest that longitudinally amphipathic .alpha.-helical peptides may function better as T-cell determinants than the other peptides investigated.

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=> s ((l7 or l8 or l9 or l10 or l11) and l2) not (l12 or l9 or l10 or l14 or l15 or l16)
L17 0 ((L7 OR L8 OR L9 OR L10 OR L11) AND L2) NOT (L12 OR L9 OR L10 OR L14 OR L15 OR L16)